AUSCULTATION OF THE HEART *

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HEART MURMURS

Mechanism, Intensity, and Pitch

WHILE arguments continue about the physical principles governing the production of murmurs, in practice both systolic and diastolic murmurs are related to three main factors: (1) high rates of flow (normal or abnormal valves); (2) forward flow through a constricted or irregular valve, or into a dilated vessel; (3) backward flow through a regurgitant valve, septal defect, or patent ductus arteriosus. These factors are frequently combined. Another which is occasionally important, and unpredictable, is the presence of some loose structure that can vibrate, as with ruptured chordæ.

While the intensity of a murmur is sometimes proportional to the degree of hæmodynamic disturbance that causes it, this is not always so, as is shown by the loudness of the systolic murmur in a small and unimportant ventricular septal defect or with slight mitral regurgitation. The loud murmur in this instance is attributed to the high velocity of the jet. Conversely, no murmur may be produced by a large flow at low velocity as through an atrial septal defect. The importance of appreciating that factors such as volume of flow and degree of stenosis may be combined is manifest in Fallot's tetralogy where the diversion of blood into the aorta diminishes the flow through the pulmonary valve so that the murmur is less loud than in pure pulmonary stenosis offering the same degree of obstruction to pulmonary flow.

Murmurs are made up of vibrations of many different frequencies (random vibrations), and exact measurements of pitch are not possible. Some generalisations, however, can be made. High-pitched, or high-frequency, murmurs are related mainly to high velocity caused by large pressure differences across small orifices, and low-pitched murmurs to low velocity and relatively small pressure differences with larger orifices. Thus, the regurgitant flow from a mildly incompetent aortic valve is at high velocity and is high-pitched. Similarly both velocity and pitch are high in a small ventricular septal defect. The pressure difference across a stenotic mitral valve is relatively small, and the orifice is large enough to take the total cardiac output: thus the murmur of mitral stenosis is low-pitched.

Systolic Murmurs

Registration of murmurs by the phonocardiograph, using much attenuation of the low frequencies so that the graph resembles the findings of auscultation (high-frequency or logarithmic phonocardiogram), gives a visual record of what is heard through the stethoscope. A murmur may be soft at the start, rising to a crescendo around mid-systole and then gradually diminishing in intensity. It is displayed on the phonocardiogram as small vibrations increasing in amplitude to a crescendo of large vibrations and then gradually diminishing in intensity (fig. 17, aortic area). This may be described as the pattern of the murmur and is found to be related to the anatomical or hæmodynamic disturbance. In one heart cycle in a particular case, varying velocities of blood-flow are responsible for changes in intensity (and therefore the pattern) of the murmur, providing that the anatomy remains constant. The blood velocity varies as the difference of pressure between two points, and so the murmur can be related to the changes of pressure in the cardiac chambers and great vessels. Changes in pressure are signalled by the first and second heart sounds, making possible a classification of murmurs by noting their timing and shape in relation to the heart sounds. This has to be based on phonocardiograms, but clinical recognition soon follows a study of these records.

A classification of systolic murmurs on these principles has been in use by some physicians for five years and seems to be satisfactory. It is based on previous investigations (Leatham 1951, 1952, Brigden and Leatham 1953, and Gray 1956), and was communicated to the British Cardiac Society in 1955:

1. Midsystolic ejection murmurs caused by the forward flow of blood through the aortic or pulmonary valves.
2. Pansystolic regurgitant murmurs due to back-flow of blood from ventricles to atria through incompetent valves, or to left-to-right shunts through a ventricular septal defect or patent ductus arteriosus.

All systolic murmurs may be divided into these two main types based on the timing of the murmurs in relation to the first and second heart sounds, though account must be taken of asynchrony between the two ventricles causing splitting of heart sounds. This applies particularly to the second heart sound. A right- or left-sided systolic murmur can only be related to valve closure on the same side.

MIDSYSTOLIC EJECTION MURMURS

Ejection murmurs swell up to a crescendo about mid-systole and invariably end before the second sound. These murmurs are caused by flow of blood through the aortic or pulmonary valves under the following conditions: (1) stenosis of valve or infundibulum; (2) increased rate

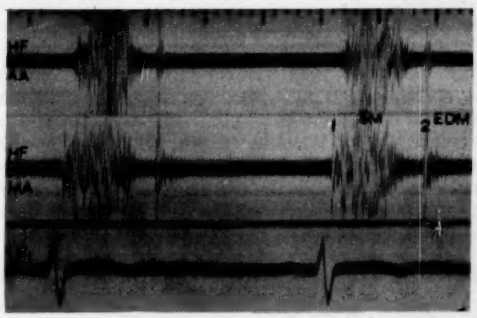

Fig. 17—Aortic stenosis.

Systolic murmur of ejection pattern finishing before aortic closure (2). The same murmur is transmitted to the mitral area, where its onset is difficult to define—probably because of an ejection sound. The ejection pattern can be appreciated best by noticing the gap between the end of the murmur and aortic closure, often most clear at the mitral area. A soft early diastolic murmur (EDM) from minimal aortic regurgitation is also shown.

* The second Goulstonian lecture for 1958, delivered at the Royal College of Physicians of London on Jan. 16. The first lecture appeared last week.

of ejection through the valve; (3) valvular damage without stenosis; (4) dilatation of the vessel beyond the valve; or (5) combinations of these factors.

There is an interval between the first sound and the onset of the murmur according to the time taken by the ventricle to raise its pressure sufficiently to open the aortic or pulmonary valve (isometric contraction time, fig. 18). The flow, and consequently the murmur, begins as blood is ejected into the great vessels, increases to a maximum about midsystole or before, diminishing during the latter part of systole, and ceases when the ventricle relaxes before the second heart sound produced by closure of the appropriate valve. There are variations in time of onset and crescendo of the murmur according to the time of onset of ejection and its rate. Ejection into the great vessels, and therefore the onset of the murmur, is earlier with low aortic or pulmonary diastolic pressures, and later with high diastolic pressures. With hyperdynamic ventricles the rate of ejection in early systole is increased, resulting in an earlier crescendo to the systolic murmur. With valve or infundibular stenosis the duration of systole of the affected ventricle is prolonged, and the crescendo of the murmur may appear to be late and may even obscure the sound of semilunar closure of the unaffected side. The murmur, however, ceases before the delayed semilunar closure of the affected side of the heart. The short crescendo of the murmur and the interval between the end of the murmur and the second sound are the characteristic and invariable features of all ejection systolic murmurs, and can easily be appreciated clinically. The gap between the first sound and the onset of the murmur, and the exact timing of the crescendo, are variable features and much more difficult to detect clinically. Thus the term midsystolic is only approximate, but serves to differentiate these murmurs from pansystolic murmurs.

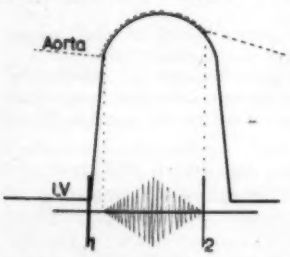

Fig. 18—Midsystolic ejection murmur.
Diagram shows the relation between the aortic systolic murmur and the heart sounds, and the left ventricular (L.V.) and aortic pressure pulses. The murmur begins when the left ventricular pressure has risen above the aortic, rises to a crescendo about midsystole, and diminishes with the flow as the ventricle relaxes.

Aortic systolic murmurs may be well transmitted to the apex and at the apex may be as loud as or louder than at the aortic area. The cessation of the murmur appreciably before the second sound (fig. 17) then distinguishes it from a mitral systolic murmur (figs. 22, 23, 28). Normally closure of the aortic valve precedes that of the pulmonary valve, and the murmur ceases before the first component of the second sound. With prolongation of left-ventricular systole from severe aortic stenosis, or left bundle-branch block, the order of valve closure is reversed and the murmur may reach the earlier pulmonary closure (in the pulmonary area) and may drown this sound, but always stops before aortic closure. The greatest difficulty in recognising the pattern of the murmur is experienced when aortic closure is soft or absent as in some cases of severe aortic stenosis. The murmur of aortic stenosis may be soft at the base if there is poor conduction from the heart to the chest wall, as in emphysema (when the heart sounds will be soft also)

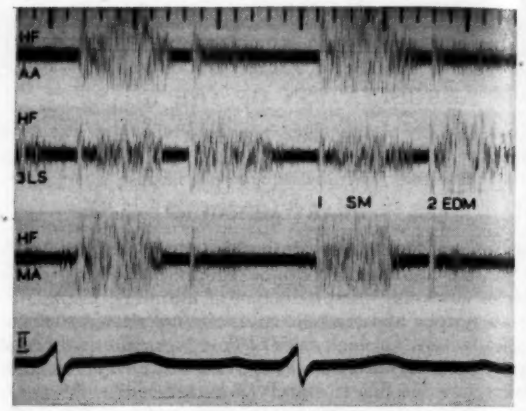

Fig. 19—Aortic regurgitation.
The ejection systolic murmur, probably mainly due to increased stroke output, is shown at the aortic area, third left space (3 L.S.), and mitral area, and is of similar shape to the murmur of aortic stenosis. The early diastolic murmur has its crescendo appreciably after aortic closure when the pressure gradient between aorta and ventricle is greatest.

and when the flow is greatly reduced—for instance, in severe left-ventricular failure or with associated mitral regurgitation (J. Shillingford, personal communication). Otherwise the murmur is always obvious, though it is frequently not intense enough to be palpable (thrill); so the presence of a slow rising pulse and hypertrophy of the left ventricle are required to make the diagnosis. In coarctation of the aorta the stenosis is more distal, and the murmur due to ejection of blood through the stenosed vessel is of the same shape as other ejection murmurs but is displaced a little later (Wells et al. 1949).

An obvious aortic ejection murmur does not always indicate stenosis, for a similar murmur is found in most patients with aortic regurgitation (fig. 19), and is related to the increased stroke output across a deformed valve, while the dilated aorta may be a third factor. Indeed, with extreme aortic regurgitation, especially when associated with an aneurysm, the systolic murmur may be sufficiently intense to be felt as a thrill. With left-to-right shunts from patent ductus, or aortopulmonary septal defect, aortic

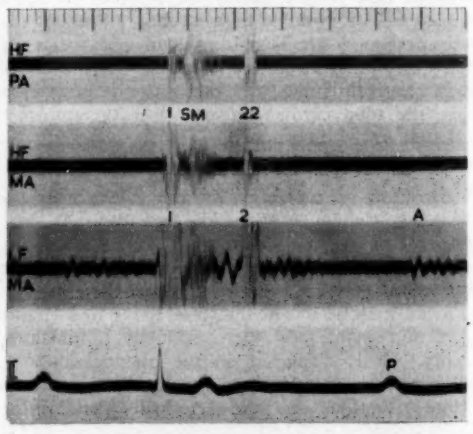

Fig. 20—Bradycardia from complete heart-block.
Moderately loud ejection systolic murmur in all areas caused by the increased stroke volume.

flow is increased, but the ejection murmur is usually drowned by the murmur due to flow through the defect unless this is very large. Murmurs due to increased stroke output of both ventricles will be discussed under the heading of pulmonary systolic murmurs.

Minimal aortic valve disease (usually rheumatic, acute, or chronic) without stenosis or incompetence causes soft ejection systolic murmurs which may be very difficult to distinguish from innocent ejection murmurs (see later). Either murmur may become moderately loud with increased stroke output from emotion or exertion. In acute rheumatic fever soft ejection midsystolic murmurs are common, but should not be attributed too readily to acute aortic valvulitis unless an aortic diastolic murmur develops (Wood 1956).

A soft or moderately loud aortic ejection murmur of no importance is often found in older subjects and is usually associated with dilatation of the aorta from atheroma or hypertension, or with thickening of the base of the aortic valve (Evans 1954); when transmitted to the apex it must be distinguished from a pansystolic murmur due to functional mitral regurgitation from left-ventricular failure, which has a very different prognosis.

Pulmonary systolic murmurs have a similar crescendo about midsystole, often a little earlier, and always finish before pulmonary-valve closure. In pulmonary stenosis, whether valvular or infundibular, there is prolongation of right ventricular systole and late closure of the pulmonary valve (Leatham 1952). The murmur may pass and bury the earlier component of the second sound, but always finishes before the delayed and soft pulmonary component (fig. 6) which can be heard in most cases and recorded in 85% (Leatham and Weitzman 1957). When severe pulmonary stenosis is associated with a large ventricular septal defect (Fallot's tetralogy), much of the right-ventricular blood is diverted into the aorta. The diminution of pulmonary flow is greater, the ejection murmur is softer (and also tends to be shorter [Vogelpoel and Schrire 1955]), and no pulmonary closure can be heard or recorded, so that the relation of the murmur to valve closure cannot then be appreciated (fig. 8). The right-to-left shunt (small compared with most left-to-right shunts) through the large ventricular septal defect is probably silent (Wood 1956). In isolated pulmonary infundibular stenosis, Mannheimer and Jonsson (1954) have suggested that the systolic murmur has an earlier crescendo than in valvular stenosis.

Increased flow into the pulmonary artery is a frequent cause of soft or moderately loud pulmonary ejection systolic murmurs. Pulmonary regurgitation as a cause of increased stroke volume of the right ventricle is relatively rare, except with high pulmonary vascular resistance. Increased pulmonary flow is more commonly due to left-to-right shunts from atrial septal defect (fig. 4) or anomalous pulmonary venous return; similar murmurs are heard in anæmia, thyrotoxicosis, and pregnancy, and with increased stroke volume from slow heart-rates as in complete heart-block (fig. 20). The rate of ejection in early systole is probably increased in all these conditions; and the crescendo of the murmur is early unless there is pulmonary hypertension, which prolongs the isometric time of the right ventricle delaying the onset of ejection and of the systolic murmur. Pulmonary systolic murmurs are occasionally transmitted to the apex, causing difficulty in diagnosis, especially in atrial septal defect when the greatly enlarged right ventricle may occupy the whole of the precordium. Differentiation of pulmonary systolic murmurs due to high cardiac outputs affecting both sides of the heart, from those due to selectively increased pulmonary flow from left-to-right shunts as in atrial septal defect and anomalous venous return, may be made by analysing the second sound in the pulmonary area. Selective increase in pulmonary flow prolongs right-ventricular systole without altering the left, and thus delays pulmonary closure but not aortic; the width of splitting of the second sound in the pulmonary area is thus increased. When the stroke volume of *both* ventricles is increased the splitting of the second sound remains normal, being obvious only during inspiration.

Since minimal pulmonary-valve disease without stenosis or regurgitation is rare, because rheumatism of this valve is rare, the only remaining cause of abnormal pulmonary ejection murmurs is dilatation of the pulmonary artery. This is almost invariably the result of pulmonary hypertension and may give rise to a soft or moderately loud ejection murmur which may be accentuated by increased stroke volume from pulmonary regurgitation and is commonly initiated by an early systolic ejection sound (see fig. 2 and Leatham and Vogelpoel 1954). These murmurs are most common with pulmonary hypertension which is primary or related to mitral-valve disease or to congenital shunts; they are less common with pulmonary hypertension due to pulmonary disease, probably because emphysema obscures the sounds at the base and the pulmonary artery is not as enlarged as in the other group. When associated with pulmonary hypertension, the murmur starts a little later than in the previous groups because the isometric contraction-time of the right ventricle is prolonged.

Basal ejection vibrations can be recorded in most normal subjects, and any slight increase in their intensity makes them audible; these are truly innocent systolic murmurs. They are always soft (at rest) and short, finishing well before the second sound, usually of similar intensity at the pulmonary, left sternal edge, and mitral areas, and often possessing a grunting or musical quality. They are most usual in children, become louder with increased blood-flow from exertion or excitement, and tend to disappear as the child grows older. Minimal aortic-valve disease produces similar soft ejection murmurs which are often maximal at the mitral area and are usually more obvious in the aortic area than are most innocent systolic murmurs. Differentiation from innocent murmurs may be very difficult, but is important for the sake of penicillin prophylaxis during dental extractions and for the early diagnosis of bacterial endocarditis, which can develop on these minimally affected valves. Differentiation of innocent ejection murmurs from pulmonary systolic murmurs due to atrial septal defect (*selective* increase in right-sided flow), or pulmonary stenosis, is made easy by analysis of the second sound, and from regurgitant systolic murmurs by their different pattern.

PANSYSTOLIC REGURGITANT MURMURS

Regurgitant systolic murmurs are always pansystolic on auscultation, and this long-established opinion is confirmed by phonocardiography (when filters are used to make the graph resemble what is heard by the ear). They are caused by flow of blood from a chamber or vessel that is at a higher pressure *throughout* systole than the receiving vessel or chamber. In mitral or tricuspid regurgitation the ventricular pressure rapidly exceeds the atrial pressure, and the backward flow and murmur

begin very soon after the first sound (fig. 21). The flow and murmur continue right up to the second sound because the pressure difference between the two chambers is still great at the time of closure of the aortic and pulmonary valves. For example, in mitral regurgitation with a systemic pressure of 120/70 mm. Hg the aortic valve must close when the left ventricular pressure is just below 70 mm. Hg. Since the pressure in the left atrium is relatively very low, backward flow must continue at this time (fig. 21). The persistence of a loud mitral murmur at the time of aortic-valve closure tends to obscure the second sound at the apex (fig. 22), though both components of the second sound are clear at the base. This helps to differentiate between mitral and transmitted aortic murmurs, provided that the third sound of mitral regurgitation is not mistaken for the second sound. Difficulty may also be encountered in severe aortic stenosis when the delayed aortic component of the second sound is too soft to be heard clinically, for the aortic systolic murmur may then appear to end with the second heart sound which is really pulmonary closure alone. A *soft* mitral murmur does not bury the second sound at the apex, and clinical recognition of its pansystolic shape is more difficult. A phonocardiogram may be necessary to decide whether this is a case of early mitral regurgitation or whether normal ejection vibrations are a little more pronounced than usual. Sometimes in mitral regurgitation the murmur is maximal in late systole, and may even appear to be confined to late systole, but early systolic vibrations can always be recorded (fig. 23). The mechanism of this late systolic crescendo is not understood, but it is diagnostic of slight or moderate mitral regurgitation. These murmurs must be distinguished from late systolic murmurs without vibrations in early systole (fig. 16), which appear to be entirely innocent and are discussed later.

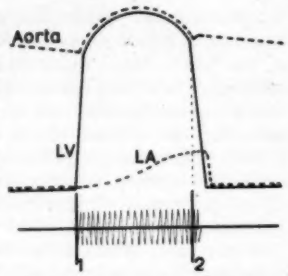

Fig. 21—Pansystolic regurgitant murmur.

Diagram shows relation of murmur of mitral regurgitation to left ventricular and left atrial pressure pulses. Owing to the great difference in pressure between ventricle and atrium the backward flow and murmur start near the beginning of ventricular systole and continue up to and past aortic closure.

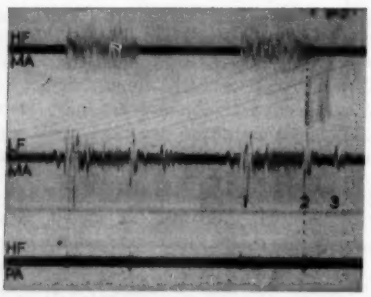

Fig. 22—Mitral regurgitation.

The pansystolic murmur continues up to and drowns the second sound on auscultation, and, on the high-frequency phonocardiogram, in the mitral area. The second sound is clear at the base (and is also shown in the low-frequency (L.F.) phonocardiogram in the mitral area).

Murmurs caused by tricuspid regurgitation are also pansystolic, often with an accentuation early in systole (Muller and Shillingford 1954). Though loudest at the lower left sternal edge they may be almost as loud at the apex when the right ventricle is greatly dilated, and are then difficult to distinguish from a mitral murmur. An inspiratory increase in intensity may be helpful, as may attention to the venous pulse. Functional tricuspid regurgitation is common in cases of severe pulmonary hypertension or right-heart failure from any cause. In atrial septal defect with high pulmonary vascular resistance, and reduced left-to-right shunt, the ejection murmur from high flow may be replaced by a pansystolic murmur at the lower left sternal edge from tricuspid regurgitation. In patients with mitral stenosis and high pulmonary vascular resistance the pansystolic murmur of tricuspid regurgitation is frequently mistaken for that of mitral regurgitation.

Some murmurs from flow through congenital shunts may be included in the group of regurgitant murmurs

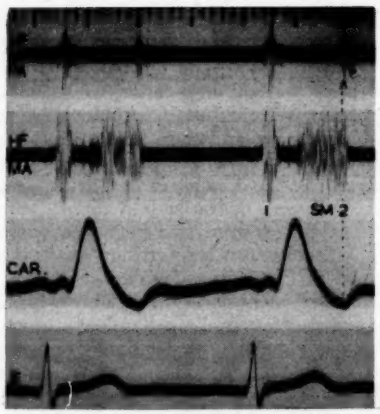

Fig. 23—Mitral regurgitation (mild).

Pansystolic murmur with late systolic crescendo obliterating the second sound at the mitral area, though it is clear at the pulmonary area.

when the blood flows back from a zone of high pressure on the left side of the heart to a zone of low pressure on the right side. Forward flow of blood (i.e., right-to-left shunt) through a ventricular septal defect or patent ductus will take place if the pulmonary vascular resistance is sufficiently high but probably never causes a murmur, for the flow is relatively small and the defect in these patients is almost invariably large. In ventricular septal defect with normal low pulmonary vascular resistance, the left-ventricular pressure is much higher than the right throughout systole, and both the left-to-right flow and the murmur are normally pansystolic (fig. 5). The site of maximum intensity at the lower left sternal edge is then the only way of distinguishing this murmur from that of mitral regurgitation unless it waxes in late systole. In ventricular septal defect with greatly increased pulmonary flow there may be an additional pulmonary ejection murmur; but this is usually hidden by the loud pansystolic murmur which overshadows it. In ventricular septal defect with high pulmonary vascular resistance, however, the pansystolic murmur is minimal or absent because the defect is large and the flow through it small; in such cases there may be an ejection sound initiating a midsystolic murmur

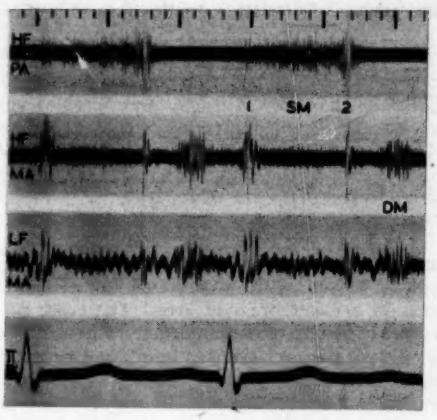

Fig. 24—Patent ductus arteriosus in a child, aged 4 years, with a rather large left-to-right shunt, and moderate elevation of pulmonary resistance.

There is a pansystolic murmur in the pulmonary area (see fig. 25 for cause). The short diastolic murmur is probably solely due to increased flow through the mitral valve.

in the pulmonary area from dilatation of the pulmonary artery (fig. 2 and Leatham and Vogelpoel 1954), and differentiation from other causes of pulmonary hypertension is difficult. There are rare patients with a loud systolic murmur at the lower left sternal edge which is confined to early systole. No disturbance of hæmodynamics can be detected, and no left-to-right shunt demonstrated. Cineangiocardiography with the injection of contrast into the right ventricle under high pressure has demonstrated a small defect low in the ventricular septum. It is possible that the unexpected pattern of the murmur is explained by the localisation of the defect to the muscular septum and by its closure when the ventricle is fully contracted (Jefferson et al. 1958).

In patent ductus arteriosus (or aortopulmonary septal defect), as in ventricular septal defect, the type of murmur depends mainly on the size of the communication and the relation between pulmonary and systemic resistances. In the newborn infant the ductus may be as large as the great vessels which it joins. Cardiac catheterisation shows that a left-to-right shunt through the duct is taking place

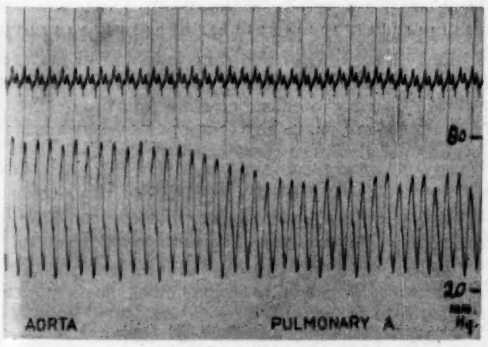

Fig. 25—Pressure pulses from the child with patent ductus (phonocardiogram shown in fig. 24).

A difference in systolic but none in diastolic pressure is shown as the catheter is withdrawn through the duct from aorta to pulmonary artery. This suggests that the maximum velocity of flow takes place in systole and the murmur would be expected to be mainly systolic.

soon after birth in normal infants (Adams and Lind 1957), but this shunt is probably small because the thick medial layers of the pulmonary arteries and arterioles of the newborn offer a high resistance to pulmonary flow (Civin and Edwards 1951); indeed the pulmonary resistance is sufficiently high to cause a reversal of flow at times (Eldridge et al. 1954, Lind and Wegelius 1954). Thus, the combination of a large duct with a small shunt is probably responsible for the absence of obvious murmurs at this stage, as in newborn lambs before the duct constricts (Dawes et al. 1955), though soft transient murmurs have been recorded in some healthy infants and presumably take place while the duct is constricting (Burnard 1958). The high pulmonary resistance usually falls, and if the duct fails to close the velocity of the left-to-right shunt gradually increases. The most common finding at this stage is a systolic murmur maximal in the pulmonary area. Phonocardiograms show that this murmur is pansystolic (fig. 24) and thus easily differentiated from a pulmonary ejection murmur (fig. 4). Catheterisation in some of these patients shows that the difference in

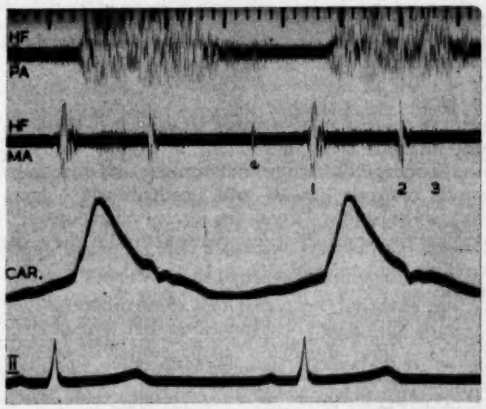

Fig. 26—Patent ductus arteriosus with normal low pulmonary resistance and large left-to-right shunt.

The flow and murmur are continuous since the difference in pressure between the aorta and pulmonary artery is great throughout the cardiac cycle. The accentuation of the murmur in late systole clearly distinguishes it from an ejection murmur (a is an artefact).

pressure between the aorta and pulmonary artery is greater in systole and may be small or absent in diastole (fig. 25). The greater velocity of blood-flow in systole presumably explains why the murmur is confined to systole. The phonocardiogram may show the murmur spilling over into diastole, and it is said that a very soft diastolic element can be heard in most of these cases (R. E. Bonham-Carter, personal communication). With increasing growth, and perhaps decrease in the relative size of the duct, and lessening pulmonary resistance, the continuous left-to-right shunt through the duct produces the characteristic continuous murmur (fig. 26). In rare cases in which the duct is unusually large the left-to-right shunt, though great, may be silent; in one case of aortopulmonary defect with large left-to-right shunt there was only a midsystolic murmur which was attributed to increased rate of ejection into the aorta. Usually with large ducts or aortopulmonary septal defects, the pulmonary resistance is high, either persisting from birth or appearing later in response to torrential pulmonary flow. The shunt is therefore small and often bidirectional. Since the duct is

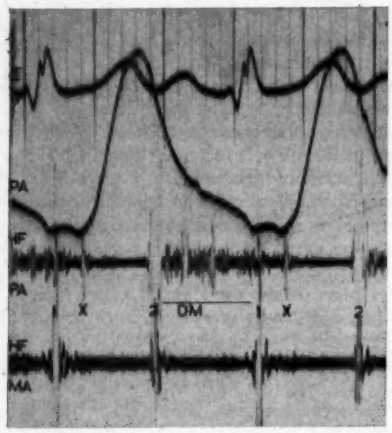

Fig. 27—Patent ductus arteriosus with balanced pulmonary and systemic resistances and pressures.

The shunts are small and bidirectional, the ductus is large, and no shunt murmurs are expected. Extreme dilatation of the pulmonary artery is probably responsible for the pulmonary ejection sound, short ejection murmur, and early diastolic murmur of pulmonary regurgitation.

large, the velocity of blood-flow through it is slow, and a shunt murmur is absent. There is usually an ejection sound, a short ejection systolic murmur, and a pulmonary diastolic murmur (fig. 27 and Leatham and Vogelpoel 1954), all resulting from the gross dilatation of the pulmonary artery almost invariably found in these cases.

INNOCENT SYSTOLIC MURMURS

It has already been stated that most innocent systolic murmurs are merely exaggerations of normal ejection vibrations and must be distinguished from other ejection murmurs. More rarely a second group of innocent systolic murmurs is encountered; these are late systolic murmurs which may be quite loud and are usually maximal at the apex (fig. 16). They tend to be initiated with a mid or late systolic click, and often vary greatly with the phase of respiration and the position of the patient. A pericardial origin has been suggested for these murmurs (W. Evans, personal communication), as for the clicks (Gallavardin 1913). A phonocardiogram may be necessary to demonstrate the absence of vibrations in early systole, for the differentiation of a pansystolic murmur with a late systolic crescendo due to minimal mitral regurgitation may be difficult.

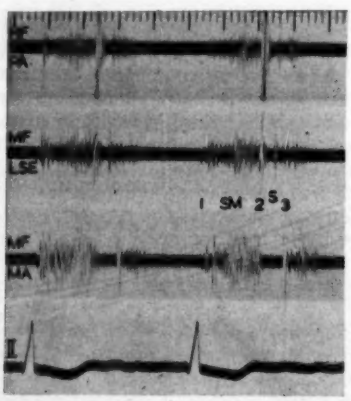

Fig. 28—Mitral regurgitation (with minimal stenosis).

The short ventricular filling murmur can be attributed mainly to increased mitral flow and is preceded by a loud third sound shown in the medium frequency (M.F.) recording from the mitral area. There is a soft regurgitant diastolic murmur in the pulmonary area and a soft opening snap (S) is heard with difficulty at the lower left sternal edge. With dominant regurgitation the snap is never obvious and is usually dwarfed by the third sound; with pure regurgitation the snap is absent.

Continuous Murmurs

Murmurs which continue throughout systole and diastole are caused by the continuous flow of blood from a higher to a lower pressure area. There are no great differences in pattern of these murmurs, whether produced in the veins of the neck (venous hum), in a patent ductus arteriosus (fig. 26) or aortopulmonary septal defect, or from bronchial-artery anastomosis in pulmonary atresia, or systemic or pulmonary arteriovenous fistulæ. Recently it has been shown that stenosis of the main branch of a pulmonary artery is associated with a continuous pressure

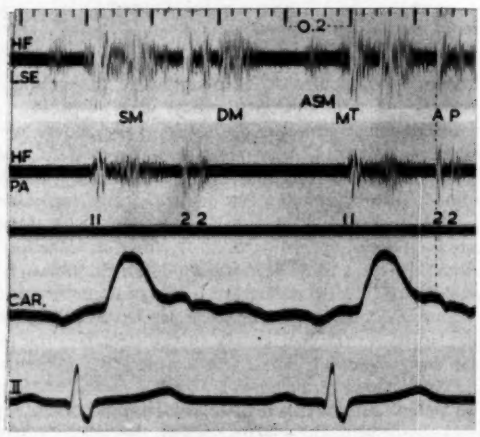

Fig. 29—Atrial septal defect with left-to-right shunt.

The right atrial systolic murmur (A.S.M.) of crescendo-decrescendo pattern is thought to be due to over-active atrial contraction ejecting blood through the tricuspid valve. The ventricular systolic ejection murmur, wide splitting of the second sound, and tricuspid diastolic murmur are also shown, and are all thought to be due to the increased flow through the right heart.

difference across the stenosis and a continuous murmur (Eldridge et al. 1957). The differentiation of aortic and pulmonary systolic and diastolic murmurs from continuous murmurs is easy because ejection murmurs diminish before the second sound (fig. 4) at a point when continuous murmurs are always of great intensity (fig. 26).

Diastolic Murmurs

Murmurs during ventricular diastole may also be classified by their timing and relation to the heart sounds:

1. Ventricular filling murmurs due to flow through the atrioventricular valves in the rapid filling phase under the following conditions:
   - Atrioventricular-valve stenosis.
   - Atrioventricular-valve disease without stenosis.
   - Increased atrioventricular flow.
2. Atrial systolic murmurs (presystolic murmurs).
3. Regurgitant murmurs from incompetent aortic or pulmonary valves.

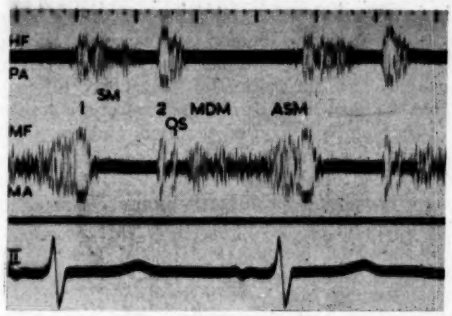

Fig. 30—Mitral stenosis.

Left atrial systolic murmur. The decrescendo is cut short by the first sound (reduced in size by voltage limitation in this recording). The mitral opening snap (O.S.) and diastolic murmur (M.D.M.) are more helpful in diagnosis.

VENTRICULAR FILLING MURMURS

Ventricular filling murmurs start appreciably after aortic and pulmonary closure when the ventricular pressure has had time to fall below that in the atrium (figs. 11, 21, 29). This well-known interval between the second sound and the onset of the murmur varies with the atrioventricular pressure relationship, but is always appreciable and has been responsible for the concise description of these murmurs as mid-diastolic; delayed diastolic is more accurate, but perhaps mitral or tricuspid diastolic is the simplest. The opening snap when present is followed usually by a short gap before the onset of the murmur as mentioned earlier (figs. 11, 30), suggesting that the snap is produced at the onset of valve movement before it opens fully. Compared with an aortic diastolic murmur the pitch of a ventricular filling murmur is always low, presumably because of the relatively small difference in pressure between atrium and ventricle and the relatively low velocity of blood-flow. The other features of these murmurs depend on the cause. In mitral (or tricuspid) stenosis the intensity of the murmur is not closely related to the degree of stenosis, since intensity depends on both stenosis and amount of flow. This explains the difficulty in hearing the murmur of mitral stenosis in patients with severe heart-failure or high pulmonary resistance and low cardiac output. The *duration* of the murmur is now widely appreciated as the best guide to the degree of mitral narrowing, since prolongation of the duration of rapid ventricular filling by severe stenosis must be accompanied by a long murmur. Unfortunately an accurate estimate of the duration of a diastolic murmur is frequently defeated by tachycardia.

Acute mitral valvulitis producing turbulence during the rapid filling phase is now thought to be the cause of the Carey Coombs murmur of acute rheumatic carditis. Experiences at the Taplow centre for acute rheumatism have emphasised the great practical value of this murmur as a sign of carditis (Wood 1950). These murmurs are soft and short, being confined to the rapid filling phase, and immediately follow the third heart sound. There may be great difficulty in deciding whether a third sound is pure or is followed by a short diastolic murmur, and a phonocardiogram may be necessary.

Left-to-right shunts from ventricular septal defect and patent ductus arteriosus cause increased mitral flow (fig. 24), and from atrial septal defect and anomalous pulmonary venous return cause increased tricuspid flow (fig. 29). The delayed diastolic murmurs heard under these conditions are thought to be caused by the high rates of flow through normal atrioventricular valves (Nadas and Alimurung 1952, Leatham and Gray 1956, Neill and Mounsey 1958); they are always short since there is no prolongation of the rapid filling phase by stenosis, and this should have prevented the mistake in the past of attributing the diastolic murmur in atrial septal defect to additional mitral stenosis. With mitral or tricuspid regurgitation, flow in the rapid filling phase is augmented, but not prolonged, and there is frequently a short mitral or tricuspid diastolic murmur following the third sound (fig. 28): distortion of valve cusps may also be playing a part. Finally, the Austin Flint ventricular filling murmur (and atrial systolic murmur), which sounds identical with that of mitral stenosis, is usually explained by assuming that the regurgitant jet from the aorta drives the aortic cusp of the mitral valve across the mitral orifice, making it vibrate (Currens et al. 1953) or producing mild obstruction.

The clinical detection of ventricular filling murmurs is best achieved with the bell stethoscope applied to the skin accurately but gently so as to avoid making tight skin into a diaphragm, for these murmurs are very low in pitch. In mitral stenosis a search must be made around the apex beat with the patient newly turned on to the left side after exertion. With tricuspid murmurs the inspiratory increase in intensity is the most valuable sign.

ATRIAL SYSTOLIC ("PRESYSTOLIC") MURMURS

Atrial systolic murmurs are also caused by atrioventricular flow during ventricular diastole, but are the direct result of active atrial contraction ejecting blood into the ventricle rather than of a passive pressure difference between atrium and ventricle. Thus the murmur is crescendo-decrescendo in shape like ventricular ejection murmurs (fig. 29). Since atrial contraction usually immediately precedes ventricular contraction these murmurs are usually presystolic in time, but the same murmur may occur in other parts of diastole if there is atrioventricular dissociation. Obvious atrial systolic murmurs are diagnostic of atrioventricular-valve stenosis, but soft ones are recorded when there is increased stroke volume of an atrium as in atrial septal defect with left-to-right shunt (fig. 29). Since contraction of the right atrium precedes that of the left, a right atrial systolic murmur is earlier than a left (about 0·09 sec. after the onset of the P wave), while the left atrial murmur of mitral stenosis may be so late (0·15 sec. after onset of P wave) that its decrescendo is cut short by the large first sound (fig. 30). The shortness of the atrial systolic murmur in mitral stenosis, and its proximity to the first sound, make it easily confused with splitting of the first sound, with an atrial sound preceding the first sound, or with an ejection sound following the first sound. It is, therefore, unwise to diagnose mitral stenosis on an atrial systolic murmur alone, particularly as it is almost invariably accompanied by an opening snap and a ventricular filling murmur. In mitral disease, however, an atrial systolic murmur is almost invariably associated with pure stenosis, and thus has its value as a sign when valvotomy is contemplated.

DIASTOLIC MURMURS CAUSED BY AORTIC OR PULMONARY REGURGITATION

Diastolic murmurs due to aortic or pulmonary regurgitation start early, immediately after closure of the incompetent semilunar valves, because of the rapid appearance

of a difference in pressure between the great vessel and its ventricle (figs. 19, 21). The murmur may swell up to a crescendo soon after the second sound (fig. 19 [3 L.S.] and Wells et al. 1949) at a time when the ventricular pressure has reached zero while the pressure in the great vessel is still almost maximal; the murmur then diminishes with the falling diastolic pressure, but continues throughout diastole (pandiastolic) (fig. 19) because of the persistent difference in pressure between the great vessel and ventricle.

Regurgitant diastolic murmurs are caused by aortic and pulmonary valve disease and aortic and pulmonary valve ring dilatation. The frequent association of regurgitation with aortic stenosis contrasts with its rarity in pulmonary stenosis and is probably explained by the very low pulmonary diastolic resistance and pressure (a few mm. Hg).

Dilatation of the aortic or pulmonary ring with regurgitation through normal valves is occasionally caused by an aneurysm of the great vessel, but is much more commonly produced by aortic or pulmonary hypertension, and pulmonary regurgitation is almost invariably secondary to pulmonary hypertension. Thus both aortic and pulmonary regurgitation are nearly always associated with a big difference in pressure across the incompetent valve. The regurgitant flow from incompetent aortic valves has been shown by dye-dilution techniques (J. Shillingford, personal communication) to be relatively small compared with the atrioventricular valves, and pulmonary regurgitant flow is likely to be on a similar scale. It follows that the relatively small regurgitant flow at high pressure has a high velocity, and these murmurs are the most high-pitched of all cardiac murmurs. They may also be the lowest in intensity and thus the most easily missed on clinical examination despite their high frequency being optimal for the human ear. A large rigid diaphragm in the stethoscope and a heart-rate which is slowing after exertion (Parkinson and Hartley 1946) provide the best conditions for hearing these murmurs. A relaxed reclining posture may sometimes be better than the sitting position. When there is doubt, the phonocardiogram is seldom found to be superior to practised auscultation, for the ear is extremely sensitive at the relatively high frequency of these murmurs. Attention must be concentrated on early diastole, especially if suspicions have been aroused by a steep rising pulse or over-active ventricle, by a soft ejection systolic murmur, or by an ejection sound. The regurgitant flow and the murmur are augmented by increased peripheral resistance, and noradrenaline has been used in doubtful cases (Besterman 1951).

With mild regurgitation causing little alteration in hæmodynamics the differentiation of aortic from pulmonary lesions may be difficult, and this again is not aided by the phonocardiogram unless the aortic and pulmonary components of the second sound are widely separated, as with bundle-branch block. The site of maximal intensity is of some value (the aortic murmur at the third or fourth left space, and the pulmonary at the second); but best of all is careful consideration of the other signs, especially the presence or absence of pulmonary hypertension.

THE STETHOSCOPE

To obtain the most from auscultation of the heart the stethoscope should transmit cardiac vibrations with minimum distortion and minimum loss in amplitude; and it should be provided with two chest-pieces—one for low frequencies, the other for high.

The great variety in design of stethoscopes indicates a remarkable diversity of opinion on what is best. Research on the efficiency of the simple acoustic stethoscope has been slight, and application of the scanty information available has been slow. It is hoped that more knowledge on this problem will soon be acquired, and the following account may have to be revised.

To minimise losses in transmission of sound the internal volume should be kept to a minimum. The optimum bore throughout the system has been shown to be $^1/_8$ in., and less than this introduces appreciable resistance to the transmission of sound (Rappaport and Sprague 1951). These statements may have to be modified for optimal transmission of high frequencies. The tubing should be as short as is practicable (say 10 in.) and the chest-piece as shallow as possible—though, with the bell variety, this is limited by the bulging of flesh into the bell. Attention should be paid to the angle and fit of the ear-pieces, and, owing to great individual variations in anatomy, this is possible only by trial of several different types. Forward angling of the lower part of the metal tubing of the head-frame compensates for some of the inconvenience of shortening the rubber tubing. Low frequencies are best transmitted with the bell applied to the chest gently so as to avoid making the skin into a rigid diaphragm, but accurately since low frequencies are easily lost through a small leak. To achieve this accuracy the edge of the bell should be rather sharp, and the diameter may need to be small to fit between the ribs of wasted patients. A larger bell has the advantage of picking up a greater volume of sound, and the advantages of both varieties can be combined in one chest-piece if a large outer bell (e.g., $1^1/_2$ in. diameter) can be made to slide over a small inner bell (e.g., $^7/_8$ in. diameter) (Leatham 1958).

A rigid diaphragm is invaluable for cutting out the low frequencies and concentrating on the high frequencies (e.g., aortic diastolic murmur and splitting of heart sounds), and its combination with a bell and a tap to switch from the one to the other has gained general acceptance. There is every advantage in using a large diaphragm (e.g., $1^1/_2$ in. in diameter) since an accurate fit on the skin is not necessary. If the large diaphragm is thin the low frequencies will be transmitted through this better than through the much smaller bell fitted to most stethoscopes, but the use of a rigid diaphragm as a filter is then lost. The combination of a large rigid-diaphragm chest-piece with a bell which can be large or small would seem to have every advantage. Diastolic murmurs which are heard best with the bell are of low frequency and therefore likely to be ventricular filling murmurs; if they are best heard with the diaphragm they must be of higher frequency and likely to be due to aortic or pulmonary regurgitation. Listening with both bell and diaphragm helps to distinguish between an atrial sound preceding the first sound and splitting of the first sound or an ejection sound. Splitting of sounds is always heard best with a rigid diaphragm, in the same way as it is recorded best in a phonocardiogram in which low frequencies are very severely attenuated.

Finally a word on electronic stethoscopes may not be out of place. These have been disappointing; the ones which I have tried do not justify the expense involved, except for deaf auscultators. Some manufacturers do not appreciate the need for severe filtration of the unwanted, high-energy, low-frequency cardiac vibrations. The residual higher frequencies need a great deal of amplification if the instrument is to prove superior to the

unaided human ear, which is very sensitive to these higher frequencies. Some instruments are even fitted with filters to reduce these valuable higher frequencies, which are so low in energy that they do not require filtration. Furthermore, the relatively enormous energy of the unwanted low-frequency cardiac vibrations produces distortion at times in most of the instruments tested. These difficulties should soon be overcome; and with the latest electronic advances, particularly in the use of transistors, small, robust, and sensitive instruments with useful variable filtration should become available. Even now some of the existing instruments are of great value in saving time during teaching by permitting large numbers of students to auscultate simultaneously with their own stethoscopes attached to the instrument. The phonocardiogram has also been displayed simultaneously on a cathode-ray tube; but this takes experience to appreciate, and a drawing of the phonocardiogram seems as useful.

SUMMARY

The graphic registration of heart sounds and murmurs has greatly facilitated analysis of their pattern, timing, and relation to hæmodynamics. Many of the principles and facts so established are being applied to auscultation with great benefit to that art.

The first and second heart sounds—valve-closure sounds—must be interpreted in the light of asynchrony between the two ventricles causing splitting of sounds. Knowledge of the degree of splitting of the second sound and its behaviour during respiration is of great diagnostic value.

Atrioventricular-valve opening sounds are always abnormal, and an obvious mitral snap is diagnostic of mitral stenosis and is very seldom absent in that disease.

Early systolic ejection sounds indicate dilatation of the aorta or pulmonary artery.

Triple or gallop rhythm is due to accentuation of ventricular filling vibrations. Atrial sounds indicate increased resistance to ventricular filling, most commonly from hypertension, and the third sound due to rapid ventricular filling is exaggerated when atrial pressure is abnormally high from ventricular failure or constriction, or atrioventricular regurgitation in the absence of stenosis.

Extracardiac sounds occur about mid or late systole, after ejection, when the heart is moving in relation to other structures but no valve movements are taking place.

Murmurs are related to flow of blood which is initiated by changes in pressure. Moments of change in pressure are signalled by the heart sounds to which the onset, crescendo, and cessation of the murmur can be related.

Systolic murmurs fell into two main groups, ejection murmurs and regurgitant murmurs, according to their shape and relation to the heart sounds:

Ejection systolic murmurs are separated from the first heart sound by the isometric contraction-time; they are crescendo-diminuendo in pattern (diamond-shaped) and finish appreciably before the second heart sound. They are due to ejection of blood from the left or right ventricle into the aorta or pulmonary artery when there is stenosis of the respective valve or outflow tract, valve disease without stenosis, or—without valve disease—increased forward stroke flow or dilatation of the aorta or pulmonary artery. Small ejection vibrations can be recorded in normal subjects, and their physiological accentuation is probably responsible for most systolic murmurs that prove to be innocent.

Regurgitant systolic murmurs are pansystolic, for they start with the first heart sound and finish with the second; the volume of sound emitted is relatively constant throughout systole or increased in late systole. They are caused by back-flow of blood through the mitral or tricuspid valve, or by a left-to-right shunt of high velocity through a ventricular septal defect or patent ductus arteriosus, the latter being modified by changes in pulmonary vascular resistance.

Murmurs which continue throughout systole and diastole are caused by the continuous flow of blood from a higher to a lower pressure area and are distinguished from ejection murmurs by their great intensity at the end of systole.

Murmurs during ventricular diastole may also be classified by their timing and relation to the heart sounds:

Ventricular filling murmurs are separated from aortic and pulmonary closure by a silent gap while the ventricular pressure is falling below the atrial level, and are most commonly due to flow through the atrioventricular valve when the valve is stenosed; both ventricular filling and the murmur are then prolonged. Atrioventricular-valve disease without stenosis, or high rates of flow through normal valves from left-to-right shunts, or overfilled atria from atrioventricular regurgitation, may produce short murmurs confined to the rapid filling phase which is not prolonged.

Atrial systolic (presystolic) murmurs are the result of atrial contraction ejecting blood through a stenosed valve or, rarely, of over-active atrial contraction—usually from left-to-right shunts.

Regurgitant diastolic murmurs start immediately after aortic or pulmonary closure and are pandiastolic. They are due to disease of the aortic or pulmonary valve or dilatation of the aortic and pulmonary valve ring from hypertension or aneurysm.

This work was started with Dr. William Evans at the London Hospital, and has been carried on with much help and stimulation from him and from the other physicians to the National Heart Hospital, particularly Dr. Paul Wood. I am also grateful to Sir John Parkinson, Dr. Alastair Hunter, Dr. David Weitzman, and Dr. John Shillingford for helpful criticism. The editor of the *British Heart Journal* has kindly given me permission to reproduce figs. 1, 2, 4, 6, 7, 11, and 29; the Editor of the *British Medical Bulletin* figs. 5, 10, and 17, and the Editor of *Circulation* figs. 20, 23, 24, 25, and 26.

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THERMAL DEATH-TIME OF SPORES IN DRY HEAT

IN RELATION TO STERILISATION OF INSTRUMENTS AND SYRINGES *

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INCREASING interest has been shown in the use of dry heat for sterilisation, but widely different temperature levels and periods of exposure have been advocated (see Darmady and Brock 1944). In Great Britain 160°C for 1 hour is usually considered suitable (Medical Research Council 1945) but the *British Pharmaceutical Codex* 1954 is content with 150°C for 1 hour. The success of conveyor-belt sterilisation by infra-red radiation suggests that higher temperatures for shorter periods will sterilise syringes equally well (Darmady, Hughes, and Tuke 1957).

Recently Kelsey (1958) has investigated the resistance of spore-bearing pathogens to moist heat, and has compared them with test organisms in common use. We here describe a similar investigation of the effect of dry heat, and make some recommendations.

Method of Investigation

To ensure reproducible temperature conditions, we used a thermostatically controlled hot-plate (20×30 cm.): at different points on its surface, temperatures were the same to within 1°C. An aluminium block (20×30×4 cm.) was placed on the hot-plate. (The two surfaces in contact had been engine-turned to ensure intimate contact). Holes had been bored in the long axis of the aluminium block to take six 2 ml., two 5 ml., and one 10 ml. Nuffield syringe-containers. The apparatus was covered by an insulator (metal and asbestos board) with a hinged door through which the containers or test-tubes could be placed in position while the block was still at the desired temperature.

Temperatures were recorded as previously described (Darmady and Brock 1954, Darmady, Hughes, and Tuke 1957). The thermocouples were as specified in B.S.I. standard no. 2648, 1955, for testing drying ovens. They were placed in small 'Pyrex' glass test-tubes (3×⅜ in.) and plugged with cotton-wool.

Before each test, a thermostat was set at the desired temperature. When the temperature of the block, as judged by a thermocouple, had remained constant and stable for at least 30 minutes a test-tube was placed in one of the cavities. Previous investigations had shown that the differences of temperature from cavity to cavity did not exceed 2°C.

The three groups of organisms used were: (1) dried soil supplied by Dr. B. W. Lacey of the Westminster Hospital (so far found to be the most resistant of the dried earths to dry heat sterilisation); (2) two non-toxigenic strains of *Clostridium tetani* (5411 and 5413) from the National Collection of Type Cultures; and (3) *Bacillus stearothermophilus*.

Soil

Approximately 0·1 g. of dried spore-bearing earth was placed in a small sterile pyrex test-tube and plugged with sterile cotton-wool. When the aluminium block had reached the desired stable temperature, the tube was placed in a cavity and a stopwatch started. The tubes reached the desired temperature (150–200°C) in 9 minutes. After withdrawal they were allowed to cool to room temperature, and the contents cultured as described by Darmady, Hughes, and Tuke (1957) except that fluid cultures were incubated for 7 days.

Tetanus Spore Suspension

The *Cl. tetani* were cultured in Robertson's medium; but although growth was good, sporulation was very poor. At the suggestion of Prof. J. W. Howie and Dr. S. T. Cowan, a modification of Tulloch's (1931) medium was then tried:

Nutrient broth was inoculated with a fæcal strain of *Escherichia coli*, incubated for 5 days, and then autoclaved at 10 lb. for 15 minutes (115°C). The autoclaved broth was then substituted for the fluid part of a universal container of Robertson's medium and inoculated with *Cl. tetani*. Growth and sporulation were excellent after 3–5 days, and this suspension was used throughout the experiments. (Both strains could be killed by 5 minutes in steam at 121°C.)

Drops of this suspension were placed on small sterile glass slides (1×¼ in.) and dried in an incubator for 1 hour at 60°C. The dried slides were then put in the test-tubes. After withdrawal from the hot-plate the tubes were allowed to cool and the slides were then dropped into bottles of Robertson's media and incubated for 7 days at 37°C. Subcultures were then made on to blood-agar plates and incubated anaerobically for 24 hours.

Stearothermophilus Suspension

The method of preparation was essentially that recommended to us by Alder and Gillespie (1957):

2 ml. of a spore suspension of *B. stearothermophilus* was heated in an oil-bath for 10 minutes at 115°C and immediately cooled. It was then added to about 8 ml. of dextrose tryptone broth, containing bromcresol-purple indicator, and incubated at 60°C overnight until the growth showed turbidity and acid production. The culture was then centrifuged at 3000 r.p.m. for 30 minutes and resuspended in 5 ml. of sterile tap water.

This new suspension was flooded over the surface of about 50 ml. of tryptone-'Lemco'-agar which had solidified on the welled side of a 250 ml. Roux flask lightly plugged with cotton-wool. The Roux flask was placed in a 60°C incubator for 7 days with the agar layer uppermost. Drying of the agar was prevented by adding a little sterile distilled water every other day to the lower part of the flask.

After 7 days' incubation the growth was examined for spore production and if satisfactory was washed off with 50 ml. of sterile tap water, filtered through a layer of sterile non-absorbent cotton-wool into a screw-capped bottle containing glass beads, and thoroughly shaken for at least 5 minutes, to break up clumps of spores. It was then heated in a boiling water bath for 15 minutes.

Examined on dextrose-tryptone-agar by the method of Miles and Misra (1938) a satisfactory suspension gives a count of at least 600,000 spores per ml. Spores were killed by 10 minutes in steam at 121°C but not by 5 minutes.

5 drops (approx. 0·1 ml.) of the spore suspension were placed in the bottom of test-tubes and dried for 3 days over phosphorus pentoxide in a vacuum desiccator. The tubes were lightly plugged and stored at room temperature in the dark. (Drying reduced the spore-count by about 75%).

After withdrawal from the hot-plate the test-tubes were cooled and the deposit in them was resuspended in 4 drops of

* From a report to the Medical Research Council Working Party on the Sterilisation of Syringes.

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TABLE I—DRIED SOIL

| Temperature | Minutes after reaching desired temperature | | |

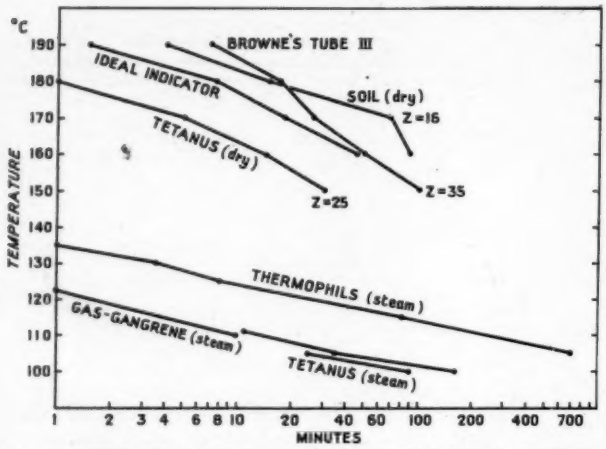

Fig. 1—Thermal death-times plotted semilogarithmically and compared with results with Browne's tubes III.

(1956), using an aluminium block, made observations with hay-dust suspension and *Bacillus licheniformis* which are in close agreement with ours for *Cl. tetani*.

Knight Oag (1940) investigated the thermal death-times of three strains of *B. anthracis*, as well as a strain of *Cl. welchii* and *Cl. septicum*. These were placed in a long quartz tube surrounded by heating elements; but, as the diameter of the tube is not mentioned, we do not know how close the heat source was to the slides used for the spore suspension. The time required to kill anthrax spores is given as 60 minutes at 120°C, 9 minutes at 160°C, 3 minutes at 185°C (determined in electric oven), $2^1/_2$ minutes at 228°C, and 2 minutes at 288°C. *Cl. welchii* and *Cl. septicum* needed 7 minutes at 170°C, and 2 and $2^1/_2$ minutes at 263°C.

At first these figures seem to be at variance with our own and those of Francis (1956). But Oag did not allow for the time taken for the slide to reach the desired temperature.

To test this, slides of the size he used ($3 \times {}^1/_2$ in.) were placed in the cavities of the block, and the ball of the thermocouple was fixed to the slide with a paper-clip. When the temperature of the block was fixed at 120°C the time taken by the slide to reach that temperature was about $4^1/_2$ minutes, and a similar time was taken to reach any desired temperature (see fig. 2). If these times are deducted from those given by Oag, the holding-time necessary for death of anthrax spores becomes $55^1/_2$ minutes at 120°C and $4^1/_2$ minutes at 160°C, and the organisms could not survive 185° for more than 1 minute. The fact that the slide took $4^1/_2$ minutes to reach the desired temperature may also explain the spores' apparently excessive resistance at higher temperatures.

Oag (1940) quotes the thermal death-time for *B. anthracis* as $2^1/_2$ minutes at 228°C and $1^1/_2$–2 minutes at 288°C; but, with the hot-plate set at 228°C, the slide would take about 2 minutes to reach 185°C and with the hot-plate at 288°C it would still take about 1 minute. If these figures are deducted from the thermal death-times given by Oag, we find that the organisms were killed in less than 1 minute after 185°C had been reached.

If the corrected figures for the thermal death-times of *B. anthracis* are plotted on semilogarithmic paper, the lines joining the thermal death-times at various temperatures are almost parallel to those of *Cl. tetani* but a little below them (fig. 3). If the figure for the thermal death-time of *Cl. welchii* and *Cl. septicum* at 170°C is similarly corrected, it becomes $2^1/_2$ minutes, which is below that of *Cl. tetani*.

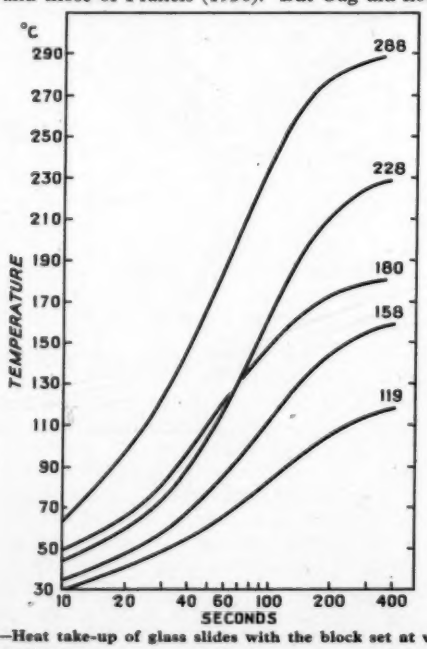

Fig. 2—Heat take-up of glass slides with the block set at varying temperatures.

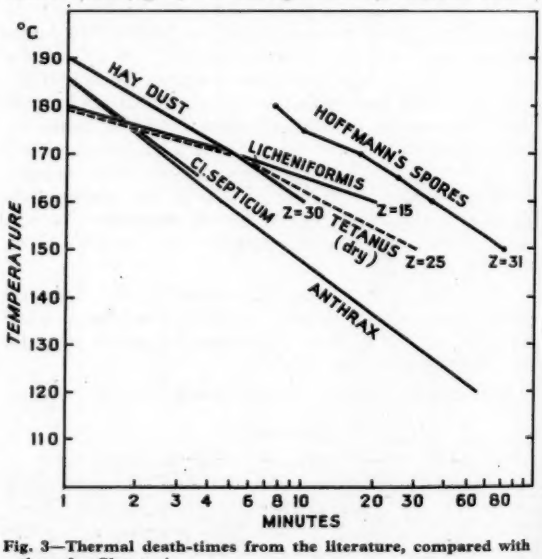

Fig. 3—Thermal death-times from the literature, compared with those for *Cl. tetani*.

Recently Gerhards (1952), using a different technique, has determined the thermal death-time of two non-pathogenic sporing organisms "Hoffmann's spores" and the "native erdesporon".

The heat source was an electric oven with a fan, and the temperatures of the metal rings used for holding the spores were measured with thermocouples. In expressing the result, the time taken for the object to reach the desired temperature was deducted from the sterilising-time. These results are plotted in fig. 3. It will be seen that, whereas the Hoffmann's

TABLE V—HOLDING-TIMES RECOMMENDED

Temperature	Time recommended (minutes)	Colour change in minutes (Browne's tube III)
150°C	—	91
160°C	45	51
170°C	18	26
180°C	7½	17
190°C	1½	7

spores are a little more resistant than *Cl. tetani* (though less resistant than dried soil) the erdesporon is less resistant. However the line joining the thermal death-times is almost parallel to that of *Cl. tetani*. Gerhards also found that temperatures below 140°C did not kill all spores.

The figures given above suggest that, of all pathogens, *Cl. tetani* is probably the most resistant to dried heat; so standards for the time-temperature ratio can reasonably be based on the behaviour of this organism. Artificially produced dried soils vary in their thermal resistance (Kelsey 1958), and in any case they will seldom be the source of contamination of surgical instruments and syringes. The extra safety margin given by using dried soils in tests may be attractive, but it must lead to the use of excessive heat, which is almost certainly injurious to a cutting edge and to certain parts of syringes (Gerhards 1952). Hence we favour a safety margin based on results with *Cl. tetani*. When deciding what such a margin should be, it is usual to say that the heat applied for routine purposes should be 1½ times what is needed to kill the organisms. Unfortunately the heat of objects placed in a hot-air oven, even of the most accurate design, may vary by as much as 5°C. We therefore suggest that, to provide an added margin of safety, the time for which instruments and syringes are kept at the chosen sterilising temperature should be 1½ times the time required to kill all organisms at a temperature 10°C lower than the one which is being used. For example, if they are to be sterilised at 170°C, the holding-time at that temperature should be 18 minutes—i.e., 1½ times the minimum lethal time for *Cl. tetani* at 160°C. (fig. 1).

This standard also has the advantage that Browne's tube III gives an added safety margin for articles sterilised by dry heat, though this may seem somewhat excessive at temperatures above 170°C.

The recommended times are shown in table V.

Summary

In 1472 experiments the thermal death-times of *Clostridium tetani*, dried soil, and *Bacillus stearothermophilus* have been determined at temperatures ranging from 150°C to 190°C. For this purpose, a thermostatically controlled aluminium block, with accuracy of ±1°C, was used as a heat source. Thermocouples were used to ascertain the temperatures. The results, plotted on semilogarithmic paper, are essentially linear. They agree with those previously reported for other spores, though in some cases a correction factor has had to be applied to allow for the time taken by the test article to reach the sterilising temperatures.

New standards for sterilisation by dry heat are proposed. The safety margin will be adequate if the articles to be sterilised are kept at the sterilising temperature for 1½ times as long as is necessary to kill all spores of *Cl. tetani* at a temperature 10°C lower. For routine use, Browne's tube III give an adequate guide to safety, except perhaps at temperatures above 170°C.

We should like to thank the South West Regional Hospital Board for providing an expenses grant, and the Nuffield Provincial Hospitals Trust for the loan of the thermocouples used in this work. We are also grateful to Mr. R. Barrington Brock, director of Messrs. Townson & Mercer, for providing the aluminium block and the thermostatically controlled hot-plate; to Dr. S. T. Cowan of National Collection of Type Culture for the two strains of *Cl. tetani*; and to Mr. V. G. Alder and Dr. W. A. Gillespie for the strain *B. stearothermophilus*.

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STERILISATION BY CONDUCTED HEAT *

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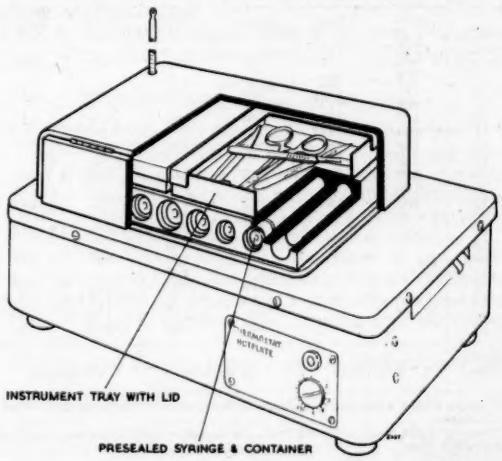
HOT-AIR ovens, though admirably suited to the sterilisation of syringes and cutting instruments, take time to reach sterilising temperature. The infra-red steriliser is ideal where syringes are needed in large numbers, but it is not quite so suitable for cutting instruments, such as stainless-steel scissors, which have a highly polished surface and therefore take up heat slowly. Hence neither the infra-red steriliser nor the hot-air oven is really practical for the small user. In considering possible alternatives, we thought that conducted heat might prove more satisfactory and more reliable.



We have used a thermostatically controlled hot-plate measuring 20×30 cm.: at different points on its (engine-turned) surface, temperatures differ by ±1°C. On the hot-plate we put an aluminium block (20×30×4 cm.), also with an engine-turned surface. In the long axis of the block are holes which take six 2 ml., two 5 ml., and one 10 ml. Nuffield containers made of aluminium. Cutting instruments can be placed in a covered tray laid

* From a report to the Working Party of the Medical Research Council on the Sterilisation of Syringes and to the Research Subcommittee of the South West Metropolitan Regional Hospital Board.

on the top of the block, and the whole apparatus is enclosed in an insulator which in the latest model is made of resin-bonded glass fibre. A hinged door in this allows syringe-containers and instruments to be placed in position while the apparatus is hot (see figure).

Except where stated, temperatures were recorded with a thermocouple placed in the plunger of the syringe (Darmady, Hughes, and Tuke 1957). For scissors and scalpels, the ball of the thermocouple was held in contact with the blade by means of a paper-clip. In testing forceps, it was held in the jaws of the forceps, and the handles locked.

The method of bacteriological investigation was as described by Darmady, Hughes, and Jones (1958) except that *Clostridium tetani* was the only test organism used.

When the hot-plate was raised to 250°C or higher heat was transferred rapidly to the syringes and instruments. But at the end of the appropriate sterilising period their temperature was often well over 200°C, and this was thought likely to damage them. When, on the other hand, the plate was set at 160°C, the sterilising temperature was obtained rather slowly. We therefore decided to fix the temperature of the plate at 190°C, which would give a rapid heat uptake with little likelihood of damage.

The heating of syringes placed directly on top of the hot-plate and covered by the insulating lid proved to be very irregular, and we concluded that the syringes must be placed, in their sealed containers, in the cavities of the aluminium block.

TABLE I—HEAT TAKE-UP OF VARIOUS SYRINGES AND INSTRUMENTS WITH ALUMINIUM BLOCK SET AT 190°C

Minutes	Syringes inserted in block		Instruments in lidded tray on top of block			
			Laid flat on bottom of trays		Laid crossways on top of others	
	2 ml.	10 ml.	Scissors	Scalpel	Scissors	Scalpel
5	154	141				
6	165	155	108	145	81	125
7	173	165				
8	177	172	130	160	102	142
9	**181**	177				
10	183	**181**	146	168	120	153
11	185	184				
12	187	185	155	159	132	161
13	188	187				
14	189	188	166	176	143	167
15	189	189	170	178		
16	**190**	**190**	172	178	152	171
17			174	179		
18			175	179	160	175
19			176	**180**		
20			178	180	165	177
21			179	180		
22			179	180	170	178
23			**180**	180	171	179
24			180	180	173	**180**
25			180	180	173	180
Sterile after	18 minutes		25 minutes		25 minutes	

Tetanus slides were removed from syringes after 18 minutes and cultured for 7 days.
Tetanus slides were removed from instruments after 25 minutes and cultured for 7 days.

Table I shows that with the hot-plate at 190°C all the syringes reached 180°C±4°C in 10 minutes, and 190°C within 16 minutes. The instruments (placed in a tray not more than $^1/_4$ in. deep, covered with an insulating lid) reached 180°C in 23 minutes, but 190°C could not be obtained. It is important that the instruments are not placed one on another.

Though it is highly desirable that the hot-plate should be maintained at 190°C, it may sometimes have to be used to sterilise from cold. Table II shows that the syringes took 22 minutes to reach 180°C and 24 minutes to reach 190°C, while the instruments took 38 minutes to reach 180°C.

TABLE II—HEAT TAKE-UP OF VARIOUS SYRINGES AND INSTRUMENTS WITH ALUMINIUM BLOCK STARTING FROM COLD

Minutes	Syringes inserted in block		Instruments in lidded tray on top of block			
			Laid flat on bottom of trays		Laid crossways on top of others	
	2 ml.	10 ml.	Scissors	Scalpel	Scissors	Scalpel
15			88	113		
20	176	178	138	160	125	157
22	**182**	**183**	152	170		
24	**190**	**190**	163	175	147	171
26	191	192	170	178	155	175
28			174	179	163	177
30	192	192	177	179	167	178
32	192	192	178	179	170	**180**
34			178	179	173	180
36			179	**180**	175	180
38			**180**	180	176	180
Sterile after	32 minutes		40 minutes		40 minutes	

Tetanus slides removed from syringes at 32 minutes and cultured 7 days.
Tetanus slides removed from instruments at 40 minutes, cultured 7 days.

The previous paper (Darmady, Hughes, and Jones 1958) showed that *Cl. tetani* were killed at 180°C in 1 minute, and advised that, to give a margin of safety, exposure to dry heat should be $7^1/_2$ minutes at 180°C or $1^1/_2$ minutes at 190°C. On this basis, if the hot-plate is set at 190°C the syringes can be safely sterilised in 18 minutes—which allows $10^1/_2$ minutes for them to reach 180°C. For instruments placed in a tray with a lid the corresponding time is 30 minutes, which allows 23 minutes for heating up and 7 minutes for sterilisation. If the hot plate is switched on from cold, syringes will need 30 minutes and instruments 45. To make sure that a particular steriliser is providing heat at the required levels it may be tested, from time to time, with Browne's tubes III.

Summary

For the small user a thermostatically controlled aluminium block, with holes which take syringes in their containers, is a reliable means of sterilisation.

Cutting instruments can be sterilised by laying them in a covered tray placed on top of the block.

With the block maintained, as recommended, at 190°C, syringes should be heated for 18 minutes and instruments for 30. If the block is started from cold, syringes will need 30 minutes and instruments 45.

Our thanks are due to Mr. R. Barrington Brock, director of Messrs. Townson & Mercer, for the thermostatically controlled aluminium block, and to Mr. E. H. Fagg of the Ministry of Health, and Mr. C. F. M. Fryd of the Department of Government Chemists, whose suggestion led to this investigation. We are also grateful to Mrs. S. East for the drawing. Finally we wish to thank the South West Metropolitan Regional Hospital Board for an expenses grant.

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"... Are not the great questions of social medicine to be found in the impact upon Western medicine of the developing countries of the East? This is the challenge that medicine has to face, of which it seems scarcely aware, so preoccupied is it with the increasingly difficult and decreasingly useful task of grafting a few more years on to the end of life. The problem of adding thirty years to the expectation of life in Africa is not as intellectually stimulating as that of adding three in Europe, but it matters more."—D. A. PYKE, *New Statesmen*, Sept. 27, 1958, p. 422.

SPIROMETRY AND EFFORT TOLERANCE IN DISEASES OF THE HEART AND LUNGS

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WHEN a patient complaining of effort intolerance is found to have both heart-disease and chronic bronchitis and emphysema, it may be difficult to decide from clinical examination alone whether the disability is due largely to the heart-disease or largely to the lung-disease. Successful treatment depends on a correct decision. This is particularly important when heart surgery is being considered.

The decision would be greatly influenced by an assessment of cardiovascular function based on the results of clinical examination and cardiac catheterisation. Experience has shown that the nature and severity of the heart lesion, and the effort intolerance it would be expected to cause, can be fairly accurately estimated in this way.

Similarly, the decision might be influenced by an assessment of lung function based on the results of clinical examination and lung-function tests. Clinical examination of the respiratory system is fallible (Fletcher 1952). A suitable lung-function test would assess the severity of the lesions of chronic bronchitis and emphysema in terms of the effort intolerance they cause, thus distinguishing the contribution of lung disease to total disability. The use and limitations of a single simple lung-function test for this purpose have not yet been described.

TABLE I—PATIENTS STUDIED, CLASSIFIED ACCORDING TO DISEASE GROUP

Disease group	Men	Women
"Bronchial disease"	296	66
Heart-disease	49	45
"Bronchial disease" and heart-disease..	30	14
Pulmonary fibrosis	14	20
Normal	34	12

The measurement of timed forced expiratory volumes (Tiffeneau et al. 1949) is probably the best measure of obstructive airway disease. It is certainly the simplest. Healthy people can expel approximately 80% of their vital capacity during the first second of a forced expiration. In patients with obstructive airway disease this proportion is reduced (Gaensler 1951, Drutel and Dechoux 1952). That this reduction is proportional to the associated loss of effort tolerance has not yet been shown. Indeed, the probability has even been denied (Stuart-Harris and Hanley 1957).

This study was undertaken to seek such a relationship, and to discover its use and limitation in assessing the contribution of obstructive airway disease to effort intolerance when heart-disease is also present.

Material and Methods

534 patients were studied. Almost all were aged 25–65. The great majority lived and worked in the East End of London (table I). They were collected in groups from out-patient clinics, breathing-exercise classes, and wards as the opportunity for investigation offered itself; there were also patients referred for lung-function study. All patients in each disease group (table I) were included.

The "bronchial disease" group includes all those with one or more of the following symptoms when these could not be explained in any other way: cough, sputum, wheeze, and effort breathlessness. No attempt was made to distinguish "bronchitis", "emphysema", or "asthma". We inferred that all these patients had narrowing of the airways—the bronchi, the bronchioles, and the alveolar ducts. The "heart-disease" group had clear clinical evidence of heart-disease with no evidence of airway obstruction, and there was no reason to suspect it: most of them had mitral-valve disease and were being studied with surgical treatment in view. The patients with "bronchial disease" associated with heart-disease had clear evidence of heart-disease, most of them with the mitral-valve involved, and, in the opinion of their physicians, also had "chronic bronchitis" or "chronic bronchitis and emphysema" or "asthma". Patients with effort intolerance due to ischæmic pain were not included. A few patients with pulmonary heart-disease were included in the "bronchial disease" group. Patients in the pulmonary-fibrosis group were so diagnosed from the characteristic appearance of their chest radiographs. Obstructive airway disease was a common complication of their condition.

The male controls were ambulance drivers free of bronchitis. Female controls were fit non-professional hospital workers.

Method

Each patient was seen by one of us and symptoms were recorded. Effort tolerance was graded in accordance with the answers to simple standard questions (table II). An attempt was made to find out what the patient actually achieved, not the severity of resulting breathlessness.

In presenting our results we have combined grade 0 with grade 1 and grade 3 with grade 4 as their relationships to the results of spirometry were similar. There are, then, three grades of effort intolerance (table II) which we consider sufficient for this study: mild, moderate, and severe. Grade 2 (mild/moderate) has been left to show the gradation from mild to moderate disability in terms of spirometry.

In each patient the following measurements were then made with a recording spirometer of the pattern described by Bernstein et al. (1952):

Forced vital capacity (F.V.C.): the maximum volume of air forced out after a full inspiration.

First-second forced expiratory volume (1 sec. F.E.V.): the volume of air forced out during the first second of a forced expiration after a full inspiration.

Forced expiratory ratio (F.E.R.): $\frac{\text{1 sec. F.E.V.}}{\text{F.V.C.}} \times 100$

Each volume recorded was the better of two attempts. If the two measurements differed greatly or if there was reason to believe that cooperation was poor the measurement was repeated. All volumes were recorded at ambient temperature and pressure (Needham et al. 1954). The subjects were seated. The test could be completed in less than five minutes.

The F.E.R. of healthy people is independent of age, stature, and ambient temperature and barometric pressure (Pemberton and Flanagan 1956). It tends to be higher in women, probably because they expel a smaller vital capacity than men of the same height.

We have used the term forced expiratory ratio to distinguish

TABLE II—EFFORT-TOLERANCE GRADES

Grade	Capacity	Grouping in present study
Normal	Healthy ambulance drivers and hospital employees	Normal
0	Able to hurry up slopes, may or may not complain of breathlessness on severe exertion or productive cough, or both	Mild
1	Unable to hurry up slopes; can hurry on level	
2	Unable to hurry on level; can maintain ordinary walking pace	Mild/moderate
3	Unable to maintain ordinary walking pace on level, but can walk for over half an hour or "about a mile" at own speed without stopping	Moderate
4	Unable to walk slowly on the level for more than quarter of an hour, or a "few hundred yards" without stopping	
5	Unable to walk one hundred yards slowly on the level, or must stop after two or three minutes' slow walk	Severe

the forced expiratory volume expressed as a percentage of the forced (expired) vital capacity from the forced expiratory volume expressed as a percentage of the vital capacity slowly expired or slowly inspired. The term would be an addition to those suggested by the Thoracic Society (Gandevia and Hugh-Jones 1958). The F.E.V. as a percentage of the slow vital capacity would have been at least as valuable for our study as the F.E.R.

Scatter diagrams were made relating effort-tolerance grading to the F.E.R. in each disease group (figs. 1 and 2).

Results

The mean F.E.R. of the patients with heart-disease fell but little with loss of effort tolerance, however severe. The mean F.E.R. of the patients with "bronchial disease" fell proportionately with their loss of effort tolerance (fig. 1). The scatter diagrams show clearly that the distinction could be considered clinically significant in the individual patient only if his effort tolerance were moderate or severe (fig. 2).

In these more severely disabled patients (unable to maintain normal walking pace) the great majority of those with heart disease had an F.E.R. of *more than* 60% (men) or 65% (women). In contrast, the great majority of patients with "bronchial disease" in this disability group had an F.E.R. of *less than* 60% (men) or 65% (women) (figs. 1 and 2). Patients with both diseases occupied an intermediate position. It is therefore suggested that when both heart-disease and "bronchial disease" are found in the same patient the probability that heart-disease is the main cause of moderate or severe effort intolerance increases as the F.E.R. exceeds 60% (men) or 65% (women). Similarly, as the F.E.R. falls below 60% (men) or 65% (women) and approaches 40%, so it becomes more probable that "bronchial disease" is the main cause of effort intolerance.

Discussion

The vital capacity falls in both heart-disease (Peabody and Wentworth 1917) and bronchial disease (Hutchinson 1846). The fall in the first-second forced expiratory volume was much greater in "bronchial disease" (because of airway obstruction) than in heart-disease (fig. 3). Hence the value of the F.E.R. in distinguishing the two conditions.

There was no evidence that the heart-disease, by lowering the F.V.C., masked the influence of bronchial disease on the F.E.R. when both were present. This was confirmed by study of 28 patients with both diseases in whom it was possible to compare assessment of the lung lesion by spirometry with assessment of the heart lesion by cardiac catheterisation or cardiotomy or both.

When patients have both "bronchial disease" and heart-disease, worsening of either condition can produce a greater increase in disability than would be expected from the apparent clinical severity of the attack if it had occurred alone. Cardiorespiratory failure due to pulmonary heart-disease or cardiac lung-disease is often found in these patients.

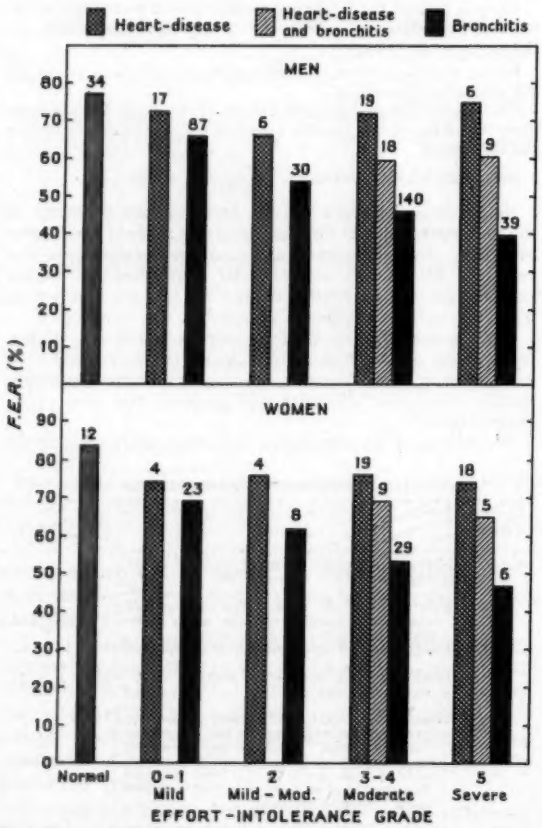

Fig. 1—Block diagram showing mean F.E.R. of each effort-intolerance grade of patients in fig. 2 with heart-disease, "bronchial disease," or both.

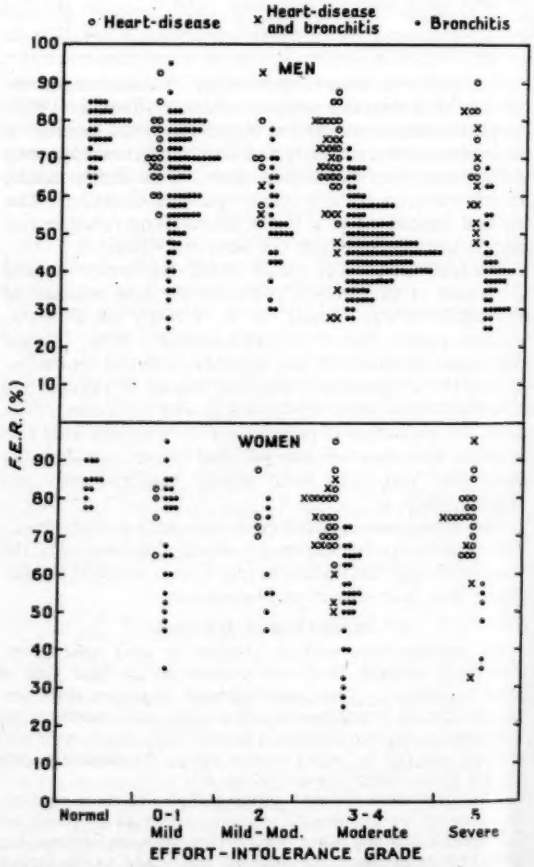

Fig. 2—F.E.R. related to effort intolerance in patients with heart-disease, "bronchial disease," or both.

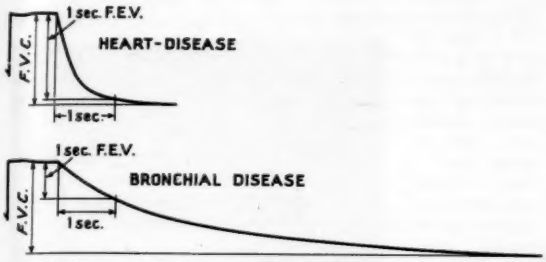

Fig. 3—Forced expiratory spirogram of 2 patients unable to walk 100 yards and with reduced vital capacity, showing reduction of F.E.R. in "bronchial disease" ("trapping") but not in heart-disease.

In the patient with heart-disease (aged 64)

$$\text{F.E.R.} = \frac{1870 \text{ c.cm.} \times 100}{1950 \text{ c.cm.}} = 97\%.$$

In the patient with bronchial disease (aged 50)

$$\text{F.E.R.} = \frac{800 \text{ c.cm.} \times 100}{1920 \text{ c.cm.}} = 42\%.$$

The effort-tolerance grades mild, moderate, and severe, which we have shown to be fairly well related to the results of simple spirometry, probably closely resemble Fletcher's (1952) dyspnœa grades 2, 3, and 4 respectively:

Grade 2.—Patient able to walk with normal men of own age and build on the level but unable to keep up on hills or stairs.

Grade 3.—Patient unable to keep up with normal men on the level, but able to walk about a mile or more at his own speed.

Grade 4.—Patient unable to walk more than about 100 yards on the level without a rest.

Hugh-Jones and Lambert (1952) have shown that in heart or lung disease Fletcher's dyspnœa grades correlate fairly well with a dyspnœa index derived from the ratio of a standardised exercise ventilation test which they described and the maximum breathing capacity. Our results suggest that in "bronchial disease" it is not necessary to take exercise ventilation into account when endeavouring to relate effort intolerance to spirometry. These results also provide further evidence of the suitability for clinical use of the work stints chosen by Fletcher in the grading he has suggested.

Spirograms made by patients with pulmonary fibrosis alone were similar to those made by patients with heart-disease. The relationship between effort intolerance and the F.E.R. distinguishes pulmonary fibrosis from "bronchial disease" in much the same way as it distinguishes heart-disease from "bronchial disease". If, as was so often the case, their breathing was wheezy, then patients with pulmonary fibrosis recorded spirograms that were similar to those of patients with "bronchial disease".

We have endeavoured to show the relationship between effort tolerance and timed spirometry in patients with disease either of the heart or the lungs, and the use and limitations of this in assessing the main cause of disability when a patient is found to have heart and lung disease together. We would call attention to the pioneer work of John Hutchinson, surgeon, in the *Medico-Chirurgical Transactions* for 1846: "On the Capacity of the Lungs and on the Respiratory Functions, with a view to Establishing a precise and easy method of detecting disease by the Spirometer."

Summary

Effort tolerance was related to the results of conventional spirometry in 500 patients with obstructive airway disease, heart-disease, or both and in 34 patients with pulmonary fibrosis.

Both the forced vital capacity (F.V.C.) and the one-second forced expiratory volume (F.E.V.) fell with loss of effort tolerance in each disease. In obstructive airway disease the one-second F.E.V. fell much more than the F.V.C. In heart-disease the two fell more or less proportionately. With loss of effort tolerance the forced expiratory ratio (F.E.R. $= \frac{\text{F.E.V.}}{\text{F.V.C.}}$ %) therefore fell little in patients with heart-disease but fell notably in patients with obstructive airway disease. The F.E.R. may thus distinguish the two conditions and point to the disease which is the major cause of disability when both are present in the same patient.

This distinction may be drawn only in moderately and severely disabled patients (unable to keep pace with their fellows on the level). In less disabled patients the overlap of results is too great for decision in the individual case, but the mean F.E.R. of groups will distinguish those with each disease.

Heart-disease and pulmonary fibrosis could not be distinguished from each other by the method.

Evidence suggests a proportional relationship between the severity of airway obstruction and the severity of effort intolerance.

We wish to thank Dr. K. Shirley Smith and Dr. R. V. Gibson for referring patients to us from the cardiac department, and the physicians and surgeons at the London Chest Hospital who allowed us to examine their patients.

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LACRIMAL AND SALIVARY PRECIPITATING ANTIBODIES IN SJÖGREN'S SYNDROME

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THE syndrome of keratoconjunctivitis sicca with rhinitis, stomatitis, pharyngitis, and laryngitis sicca, and sometimes with parotitis and a polyarthritis of the rheumatoid type (Sjögren 1933, Duke-Elder 1952), may arise in various collagen diseases or in sarcoidosis (Jones and Stevenson 1957). Although the syndrome, which is commonly designated by Sjögren's name, is regarded by some merely as a variant of rheumatoid disease (Thompson and Eadie 1956), the absence of arthritis in many cases makes it reasonable to postulate the existence of a specific disease or process which may operate independently of that which produces the joint disorder. Evidence for such a mechanism is presented in this preliminary report.

In 1956 Dr. E. T. Knudsen and I found that the serum of about half the cases we examined showed raised gamma-globulin levels, giving positive precipitation and flocculation liver-function tests. This observation, which has been confirmed in two further series (McLenachan 1956, Jones and Miller), invites a comparison with Hashimoto's thyroiditis, in which high gamma-globulin levels reflect the presence of autoantibodies to thyro-

globulin (Doniach and Roitt 1957). Several other points of similarity are striking. Both conditions affect chiefly middle-aged females. Both the thyroid and the lacrimal glands in their " normal " state are said to have lymphoid tissue scattered between the acini. In both diseases the affected glands show an eosinophilic change in the epithelium and dense infiltration by lymphocytes and plasma cells, often with lymphoid follicle formation. The epithelium degenerates amid lymphoid tissue, and the process often ends in fibrosis (Thomson 1957, Morgan and Raven 1952). Furthermore both conditions may be associated with rheumatoid arthritis (Luxton 1957).

These observations suggest the possibility that some cases of Sjögren's syndrome may have a specific autoimmune aberration—analogous with that demonstrated in Hashimoto's disease (Roitt et al. 1956, Doniach and Roitt 1957, White 1957, Witebsky et al. 1958, *British Medical Journal* 1958). Some potentially antigenic substance could leak from the acinar epithelium, and on coming into contact with lymphoid tissue produce an antibody, the action of which would damage the epithelium causing further liberation of antigen. The widespread involvement of the salivary and other upper-alimentary and respiratory glands suggests that they may all contain antigenic substances shared with the lacrimal gland. Thus the process may be triggered off from any one, after which the action of bloodborne antibody may continue the destructive chain reaction in other glands. The increase of gamma-globulin probably reflects a high level of circulating antibody during the stage of active immunological destruction of the glands. When the secretory epithelium is destroyed, leakage of antigen ceases and the gamma-globulin level falls again; but, since the lacrimal functions have been ablated, the ocular symptoms are unchanged.

Investigation

Serum from patients with keratoconjunctivitis sicca with or without other features of the Sjögren syndrome was tested against saline extracts of cadaver tissues using Halbert's modification of the Ouchterlony agar-gel diffusion precipitin test (Halbert et al. 1955). Of the first 40 sera tested, 39 gave negative results but 1 showed an equivocal reaction against the lacrimal glands of two cadavers, and against the submandibular salivary gland of one, though there was no reaction with either kidney or liver. Further work showed positive precipitin reactions with this serum (see case-report), and suggests that the absence of reaction with the remaining 39 sera does not mean that they do not contain similar antibodies.

Preliminary tests have been done with serum from 4 other patients with keratoconjunctivitis sicca. Of these, 2 had raised gamma-globulin levels and they both gave positive reactions with extracts of salivary glands from cadavers.

Case-report

A man of 44 had complained for eight years of gritty irritation in both eyes, worse when indoors in a dry atmosphere. He also gave an eight-year history of dryness of the mouth. A painful swelling of his right parotid gland had been treated by radiotherapy three years before. There was nothing suggestive of rheumatoid arthritis beyond some vague pains in his shoulders, back, and knees, cured by massage fourteen years ago.

The lower fornix of each eye contained a string of mucus. Some small follicles were present in the slightly inflamed conjunctiva. The precorneal film was thick and tenacious, and contained much debris. Schirmer's test was grossly reduced (right 4 mm., left 3 mm.: in five minutes and after simulation of the middle turbinates, right 6 mm., left 5 mm.). Bengal rose gave unequivocally abnormal staining of the interpalpebral conjunctiva of each globe, and some fine punctate staining of the lower part of each cornea.

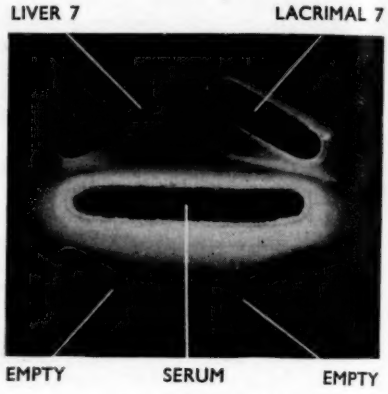

Fig. 1—Agar-gel diffusion precipitin test showing a single precipitin line between the serum and the lacrimal extract, and non-specific opacification of the agar around the serum.

Rose's test at a dilution of 1/4 was negative. No lupus erythematosus (L.E.) cells were found. Biopsy of a conjunctival follicle showed reactive lymphoid hyperplasia in the lamina propria, and there was no evidence of sarcoidosis. The total serum-protein was 6·4 g. per 100 ml., and the zinc-sulphate flocculation test gave a positive result (16 units). Electrophoresis of serum-proteins showed slight increase of gamma-globulin.

The serum gave a single precipitin line (figs. 1 and 2) with extracts of lacrimal gland from each of five cadavers tested, and with extracts of submandibular salivary gland from each of four cadavers tested (see table). A reaction of identity was observed between the line with submandibular extract from cadaver 4 and lacrimal extract from cadaver 5. Extracts of liver and muscle from all of five cadavers tested gave negative results. Kidney extracts from two cadavers gave negative results but three others gave positive results. 24 control sera submitted for Wassermann reactions gave negative results with lacrimal, salivary, kidney, liver, and muscle extracts.

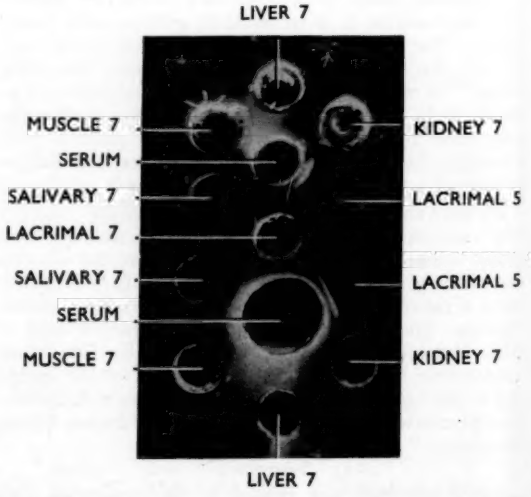

Fig. 2—Agar-gel diffusion precipitin test showing a single line between the serum and the lacrimal 5 extract. The potency of the lacrimal 7 and salivary 7 extracts had deteriorated so that lines no longer formed to these on this plate.

THE RESULTS OF PRECIPITIN TESTS BETWEEN THE PATIENT'S SERUM AND CADAVER TISSUE EXTRACTS

Cadaver no.	Lacrimal gland	Salivary gland	Kidney	Liver	Muscle	Empty control
3	+	0	−	−	0	−
4	0	+	+	0	−	−
5	+	0	0	−	−	−
7	+	+	−	−	−	−
8	+	+	+	−	−	−
9	+	+	+	−	−	−

+ =positive reaction, − =negative, 0 =not tested.

Methods

Tissue Extracts

The cadaver tissues were prepared by mincing with scissors and extracting in normal saline containing 0·03% sodium azide, in the ratio of 1 g. of tissue to either 2 ml. or 5 ml. of saline. They were frozen overnight at −30°C, thawed, ground in a tissue-grinder taking care to avoid heating, centrifuged, and stored in bulk at −30°C or in small quantities at 4°C.

Preparation of Agar

1·125 g. of New Zealand agar and 1 g. of glycine were dissolved in 200 ml. of isotonic saline by heating in an autoclave at 5 lb. for twenty minutes, then filtered through Whatman paper no. 1 and cooled to 56°C. 50 ml. of isotonic saline containing 2·06 g. of sodium barbitone was added and the pH was adjusted to 7·4 with concentrated hydrochloric acid. 25 ml. was poured into 4-in. petri dishes, allowed to set overnight, and cut into various patterns of circular wells or angled ditches (fig. 3). The moisture was extracted from the wells until extrusion by synæresis ceased, then the bottoms were sealed with 1% agar. The wells were filled with serum or tissue extract, and after one to three hours those containing serum were topped up. Filter paper under the lids of the petri dishes, kept moist with 1% formol-saline, prevented drying and infection.

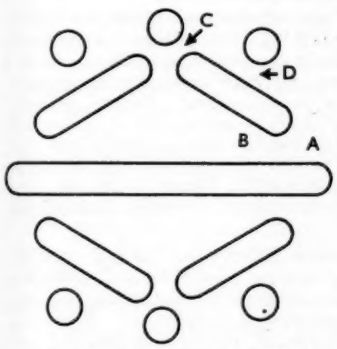

Fig. 3—The pattern of wells and ditches for the agar-gel diffusion precipitin test.

FACTORS INFLUENCING RESULTS

The Pattern of Wells

In the first 40 screening tests we used an octagonal pattern of 6 mm. wells with centres 20 mm. apart, the central well being 11 mm. in diameter (Halbert 1955). But these distances proved too great, and some of the 39 negative sera may give positive results when a different technique is used.

Apparently the concentration of antibody at a given distance is greatest when the source is a long straight ditch, and is less when it is a circular well, decreasing as the diameter decreases.

A combination of ditches 5 mm. wide and wells 5 mm. in diameter lying 5 mm. apart at their closest point and angled at 30° (fig. 3) is more sensitive than a simple pattern of circular wells. If serum is placed in the central ditch and also in the peripheral circular wells, and antigen placed in the angled ditches:

at A there is a tendency to antibody excess,
at B equivalence is approached,
at C there is a tendency to antigen excess, and
at D there is more pronounced antigen excess.

Thus, a weak serum set against a strong antigen will give a line only at A or at A and B, whereas a strong serum set against a weak antigen will give a line only at D or at D and C. In this way a roughly twofold titrational effect is produced between each position. When there is equivalence the lines will be best at B, and in this case they will also probably be demonstrable by the usual pattern of circular wells as in fig. 2.

False Lines

Non-specific opacification of the agar around the serum may obscure a weak positive, or may produce an appearance resembling a precipitin line. These false lines begin to develop around the serum within a few hours, whereas true lines take at least a day to appear. The shape of the false line is determined entirely by the shape of the serum source and by the agar available for diffusion, whereas the shape of the true lines is determined by migration of antigen and antibody in opposing directions. Buffering the agar and adding glycine minimise these effects (Halbert et al. 1955), but care is needed to avoid misinterpretation. The inclusion of a control (empty) ditch removes any uncertainty.

Agar Concentration

The viscosity of the agar is a critical factor. The gel should be as soft as is practicable to cut; this is at a concentration of 0·45% when glycine and barbitone buffer are included. Increasing the concentration to 0·65% has been sufficient to reduce a strong positive developing after one day to the faintest visible line much nearer the serum source which took three weeks to appear.

The antibody thus behaves in agar as though it were a large molecule which diffuses with difficulty if the viscosity is beyond a critical level. A similar observation has been made in Hashimoto's disease (Pressman et al. 1957).

Dilution Extracts

With glands extracted in the ratio of 1 g. of tissue to 2 ml. of saline, it was found that undiluted serum gave positive results with doubling dilutions of extracts as far as 1/4 or 1/8, and twofold dilution of serum went to 1/8 or 1/16. The number of tests which can be done with each cadaver is limited by the fact that the lacrimal glands together weigh only a little over 1 g. Cadaver 6 was extracted at 1/20 but gave negative results; cadaver 7, extracted at 1/5, was very satisfactory. Tissues from cadavers 8 and 9 were stored in bulk at −30°C and extracted at 1/5 after five weeks; these gave weak positive results, the lines developing only in position D in fig. 3.

Stability

The stability of the extracts has varied; extract 3 was active for eight months, extract 4 for five months, and extract 5 for four months. Extract 7 deteriorated rapidly between the second and third weeks, that is between the times when the plates shown in figs. 1 and 2 were set up; extract 5 meanwhile maintained its potency. Azide was not added to the first five extracts.

Discussion

The patient fully studied has circulating precipitating antibodies to extracts of lacrimal and salivary glands, but the possibility that they are isoantibodies and not true autoantibodies has not yet been excluded. It could be argued also that these antibodies were the result of glandular degeneration rather than the cause of the destruction. But the analogy with Hashimoto's disease supports the probability of an autoantibody.

The nature of the antigen is uncertain but, again by analogy, it is likely to be some major component or precursor of lacrimal and salivary secretions. It has been shown that lysozyme, which is normally present in lacrimal and salivary secretions, is constantly absent or grossly reduced in the tears in keratoconjunctivitis sicca (McEwen and Kimura 1955). This appears to be so specific that it has been suggested as a diagnostic test for early doubtful cases.

Work is in hand to elucidate these points and to determine how often antibodies are found in patients with keratoconjunctivitis sicca and the Sjögren syndrome as a whole. The significance of the positive results with some kidney extracts, but not with others, is unknown. The relation of these phenomena to rheumatoid disease is also uncertain.

Summary

Antibodies to extracts of lacrimal and salivary glands from cadavers were demonstrated by the agar-gel diffusion precipitin test in 1 patient out of 40 with Sjögren's syndrome. Analogy with Hashimoto's disease suggests that these are specific autoantibodies.

This hypothesis has since been supported by the finding of positive reactions with extracts of salivary glands in preliminary tests in 2 out of 4 additional patients with Sjögren's syndrome.

Dr. E. T. Fraud n first drew my attention to the occurrence of raised gamma-globi in in this condition. Dr. Charles Smith introduced me to the tchniques used and gave much helpful advice. Mr. T. Keith Lyle indly referred the patient whose case-history is described in detail. Dr. A. H. Miller arranged for the serum-protein estimations to be m de at the Courtauld Institute of Biochemistry, Middlesex Hospital. Dr. B. W. Lacey carried out the Rose's test, and Dr. P. B. Schofield the L.E.-cell test. I should like to thank the staff of the Bland-Sutton Institute of Pathology, Middlesex Hospital, for making cadaver tissues available, and Miss P. Edgson for technical assistance.

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LIVER IN NORMAL PREGNANCY, PRE-ECLAMPSIA, AND ECLAMPSIA

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THE liver in normal pregnancy as well as in toxæmias has attracted the attention of many workers.

Dietel (1947) observed an increased number of binucleated cells in pregnancy. Ingerslev and Teilum (1945), however, did not find any significant morphological difference in the liver of pregnancy. Dieckmann et al. (1949) found that liver-function tests were of little value in either the diagnosis or prognosis of toxæmias. Mack et al. (1951) found that in pre-eclampsia and eclampsia the mean levels of total plasma-proteins and of plasma-albumin and β and γ globulins were lowered, although the globulin fraction as a whole tended to be raised. Mukherjee and Govan (1951) found increased thymol turbidity in toxæmias, more distinct in eclampsia than pre-eclampsia. Mukherjee (1952) further found that bilirubin retention was increased in toxæmias. Sheehan (1950) described focal and diffuse types of hepatic lesions in toxæmias of pregnancy.

TABLE I—PARITY OF PATIENTS

Group	Parity								
	1	2	3	4	5	6	7	8	9
Normal	3	2	1	3	..	..	1	..	..
Eclampsia ..	5	5	2	1	..	3	..	..	..
Pre-eclampsia ..	8	3	1	2	..	..	..	..	1

There have been very few studies in which needle biopsy of liver has been correlated with liver-function tests. The present work was undertaken to obtain clinical, biochemical, and pathological data in normal full-term pregnancy, pre-eclampsia, and eclampsia.

Materials and Methods

The cases studied were admitted to Nowrosjee Wadia Maternity Hospital and B.Y.L. Nair Charitable Hospital. Cases of pregnancy in which there was no albuminuria, hypertension, or œdema and no other clinically recognisable abnormality were taken to be normal. Patients showing œdema, albuminuria, and high blood-pressure were classified as cases of pre-eclampsia. Patients who in addition had convulsions were taken to be cases of eclampsia. In this series patients with severe jaundice and in a poor clinical state were not studied, as taking needle biopsy of the liver in such patients was considered risky.

On admission the clinical history was elicited. Blood-pressure was determined and the urine examined. Blood was taken for routine hæmatological studies; plasma-proteins, serum-bilirubin, serum-alkaline-phosphatase (Bodansky), cephalin cholesterol flocculation, thymol turbidity, and non-protein-nitrogen were estimated; and the Kahn test was performed. The bromsulphalein-clearance test was performed with 5 mg. of the dye per kg. of body-weight, and clearance noted after forty-five minutes.

The patients were given 10 mg. vitamin K intramuscularly for one or two days. Needle biopsy was then undertaken under local anæsthesia, using a Vim Silverman needle. No patient had an untoward reaction. In 2 cases of eclampsia the liver tissue was obtained immediately after death of the patients. The biopsy material was fixed in 10% formol saline. Sections were stained with hæmotoxylin and eosin.

Observations

41 cases were studied: normal 10, pre-eclampsia 16, and eclampsia 15. The ages of the patients, ranging from 16 to 38 years, were evenly distributed in all the groups. The normal cases were observed in the ninth and tenth months of pregnancy. The cases of pre-eclampsia and

TABLE II—LIVER-FUNCTION TESTS

Group	Total serum-protein (g. per 100 ml.)		Serum-albumin (g. per 100 ml.)		Serum-globulin (g. per 100 ml.)		Serum-alkaline-phosphatase (Bodansky units)		Cephalin cholesterol flocculation	Thymol turbidity (units)	Bromsulphalein retention	Serum-bilirubin (mg. per 100 ml.)	Non-protein-nitrogen (mg. per 100 ml.)
	Av.	Range	Av.	Range	Av.	Range	Av.	Range					
Normal	5·8	5·5–6·2	3·6	3·4–4·0	2·6	2·2–3·6	..	..	Neg. to 1+	1–3	Nil	<1 mg.	..
Pre-eclampsia	5·2	3·5–6·2	2·75	1·1–3·9	2·48	1·3–3·0	3·5	2·3–4·2	Neg. to 3+	1–7·8	Insignificant	<1 mg.*	15–24
Eclampsia	5·56	4·2–6·9	2·89	2·1–3·9	2·67	1·7–3·7	9·8	6·5–15·2	Neg. to 3+	4–7	Insignificant	<1 mg.†	11–16

* 6·5 mg. in the case of pre-eclampsia with jaundice. † 12·4 mg. in the case of eclampsia with ? infective hepatitis.

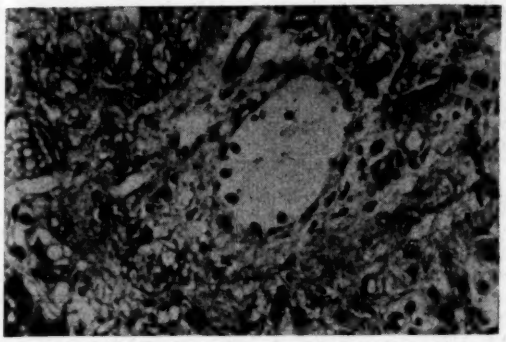

Fig. 1—Photomicrograph of liver (eclampsia) showing focal periportal lesion. There is disruption of lamina limitans and liver cell plates. (Hæmatoxylin and eosin. ×270.)

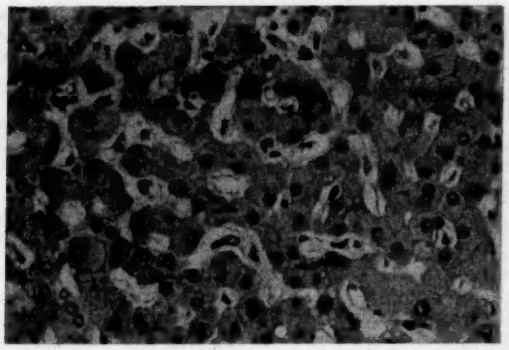

Fig. 2—Photomicrograph of liver (eclampsia) showing prominent space of Disse with poorly staining exudate. (Hæmatoxylin and eosin. ×270.)

eclampsia were studied from seventh to tenth month of pregnancy. The parity of the patients is in table I.

Nothing significant was noted in the past history of normal cases. Of the pre-eclamptic patients 2 had a history of abortion and 2 had a history of œdema in previous pregnancies. Among cases of eclampsia 1 had history of previous abortion, 1 had had fits during three previous pregnancies; while another had in previous pregnancies had fits resembling idiopathic epilepsy as they were preceded by a visual aura. The blood-pressure varied from 130 to 220 mm. Hg systolic and 90 to 150 mm. Hg diastolic in cases of pre-eclampsia and from 130 to 190 mm. Hg systolic and 90 to 140 mm. Hg diastolic in cases of eclampsia. There was jaundice of three weeks' duration in a patient with pre-eclampsia. A case of eclampsia also had jaundice of sudden onset shortly before death.

Laboratory Findings

In normal cases the urine was clear. In cases of pre-eclampsia and eclampsia there was varying amount of proteinuria, casts, and cellular exudate. Anæmia was detected in every case, but its degree differed between the various groups. The hæmoglobin ranged from 9 to 12 g. per 100 ml. in normal cases, and from 7 to13 g. per 100 ml. in pre-eclampsia and eclampsia.

The biochemical findings in the blood are shown in table II.

Histological Findings

Normal pregnancy.—The liver-biopsy material did not reveal any significant deviation from normal. Occasionally there was slight reticuloendothelial hyperplasia. In a few cases there were " light and dark " areas which have been shown to be fixation artefacts (Ingerslev and Teilum 1945).

Pre-eclampsia.—The liver was normal except for slight anisocytosis and anisonucleosis; often there was decreased stainability and eosinophilic clumping of the cytoplasm, and a significant amount of light yellowish brown pigment was present in the cells. The sinusoids contained hyperplastic reticuloendothelial cells and occasionally granulocytes. There was a distinct increase in the number of cells showing binucleation.

Eclampsia.—The histopathological features were similar to those observed in pre-eclampsia except in 5 cases, in which the following changes were found:

1. In 2 cases the changes were similar to the focal lesion described by Sheehan (1950) (fig. 1). There was profound destruction in the portal region. The lamina limitans was completely disrupted and replaced by an eosinophilic structureless mass. In the immediate periportal area there was massive destruction of liver cell plates, leaving only isolated groups of cells. The cells were reduced in size, showed evidence of necrobiosis, and had pyknotic nuclei. An appreciable number of surviving cells showed slight congestion and mononuclear and eosinophilic infiltration and prominent space of Mall. At other sites there was much exudate in the space of Disse with virtual occlusion of the sinusoidal space. Parenchymal cells around the periportal zone of hæmorrhage showed intranuclear vacuolation. There was reticuloendothelial hyperplasia, and cells contained hæmatogenous pigment. A few bile canaliculi contained inspissated bile.

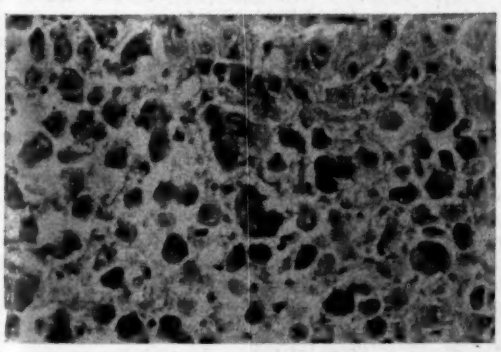

Fig. 3—Photomicrograph of liver (eclampsia) showing much loosening of cell plates, necrobiosis, and binucleation. (Hæmatoxylin and eosin. ×270.)

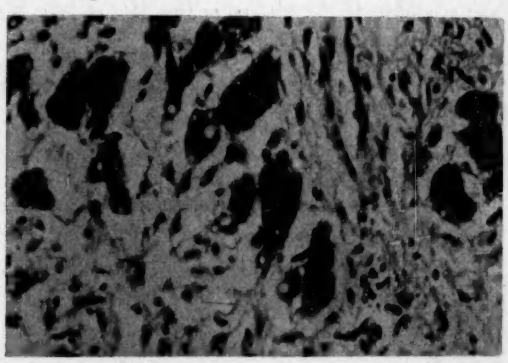

Fig. 4—Photomicrograph of liver showing gross destruction of parenchyma. (Hæmatoxylin and eosin. ×270.)

2. In 1 case the hepatic lesion was similar to the diffuse type described by Sheehan (1950). The space of Disse and space of Mall were prominent on account of a poorly staining exudate (fig. 2). Parenchymal cells showed cloudy swelling and at places necrobiosis.

3. In 1 case there was much loosening of liver cell plates and isolation of single cells or small groups of cells from each other. The cells were of various sizes and shape; some were binucleated (fig. 3). The patient died.

4. In 1 case there was gross destruction of hepatic parenchyma (fig. 4). Probably this patient, who died, had fulminant infective hepatitis.

Discussion

These data show that no significant or characteristic changes in liver structure or function are associated with normal pregnancy. There seems therefore to be no justification for the assumption that there exists a " pregnancy liver ".

In the patients with toxæmia certain features appear significant. Although the average age did not differ significantly between the various groups the patients with severe liver lesions belonged to a younger age-group. There is apparently a slightly increased likelihood of severe toxæmia with longer duration of pregnancy.

No serial number of pregnancy is immune from toxæmia. Earlier pregnancies, particularly the first pregnancy, seem to be associated with more severe grades of toxæmia.

Hæmatological values did not differ significantly between the three groups. Alkaline-phosphatase values tended to be higher in more severe grades of toxæmia. Cephalin cholesterol flocculation and thymol turbidity were grossly abnormal in some cases. Bromsulphalein retention, serum-bilirubin levels, and non-protein-nitrogen values were useless as indicators of the type or degree of toxæmia. Syphilis, judged by the Kahn test, has no ætiological significance.

It is also evident that no constant histopathological picture is associated with either pre-eclampsia or eclampsia. Increased binucleation, probably due to mitosis, was present to a significant degree in the present cases of toxæmia. Dietel (1954) has described increased binucleation in the liver of normal pregnancy, but in our series of normal cases this was not a notable feature.

The majority of cases of pre-eclampsia and eclampsia cases show only slight hepatic lesions. In 3 of our cases the lesions were similar to that described by Sheehan (1950). Sheehan believes that this lesion occurs in fatal eclampsia in the last one or two days of life. Since the majority of the cases in our series were studied by needle biopsy at an earlier period of disease, the paucity of lesions may be partly explained. According to Sheehan (1952) these lesions are found in 90% of cases in which the patient dies but in only 28% of cases in which the patient recovers. Dieckmann (1952) also found typical lesions in only a small proportion of his cases.

The loosening of liver cell plates observed in 1 of the present cases has not been previously described. In the diffuse lesions described by Sheehan, although the sinusoidal lining is stripped away from parenchymal cells, the continuity of the liver cells themselves is maintained.

The prominence of the space of Disse does not seem to be an artefact or agonal change, since in most of these cases the material was derived from antemortem biopsy. Exudation in these spaces as well as in space of Mall appears to be a destructive pathological process.

Summary

Liver function and structure were investigated in 10 cases of normal pregnancy, 16 of pre-eclampsia, and 15 of eclampsia.

Normal pregnancy does not seem to be associated with any definite alteration of hepatic structure or function.

Low parity and youth seem to predispose to severe grades of toxæmia. The symptoms, history of previous pregnancies, blood-pressure, urinary findings, and hæmatological and biochemical findings do not show any significant correlation with the prognosis.

Pronounced hepatic lesions were found in only 5 cases of eclampsia. 1 of these cases was probably of fulminant infective hepatitis; in the others the type and severity of the hepatic lesions could not be correlated with any of the clinical or laboratory data.

Exudation in the space of Disse does not seem to be an artefact or agonal change.

This investigation was supported by a Sir Mangaldas Mehta grant of the University of Bombay. Our thanks are due to Dr. K. M. Masani, P.M.O., Nowrosjee Wadia Hospital, and Dr. V. N. Shirodkar, Dr. P. C. Daroowala, Dr. B. N. Purandare, and Dr. J. N. Karande for the clinical material; and to Dr. V. R. Khanolkar, Dr. K. T. Gajjar, Dr. K. Raman, Dr. M. V. Sirsat, and Dr. D. S. Nadkarni for the biochemical tests, and Mr. R. V. Nerurkar for the photomicrographs.

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URINARY 17-KETOSTEROID AND 17-KETOGENIC STEROID EXCRETION IN SOUTH AFRICAN BANTU

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THERE is little information on urinary 17-ketosteroid values and none on 17-ketogenic-steroid values in the Bantu and other non-White races.

Barnicot and Wolffson (1952) found in 37 West Africans that the 17-ketosteroid excretion was significantly lower than among a White control group ($7{\cdot}97 \pm 0{\cdot}48$ mg., compared with $13{\cdot}7 \pm 0{\cdot}72$ mg., per twenty-four hours). Friedmann (1954) obtained similar results in his study of 23 Indians and a White control group ($10{\cdot}81 \pm 2{\cdot}32$ mg., compared with $21{\cdot}28 \pm 2.64$ mg. per twenty-four hours). Ch'en P'ei-en (1956) and Chou and Wu (1937) reported that likewise in Chinese males and females excretion was lower than in Whites. Although the methods used by the different investigators for determining 17-ketosteroids varied slightly, all were modifications of the original Zimmermann reaction.

In 1956 Kinnear undertook 17-ketosteroid determinations on 40 South African Bantu. His findings were:

11·8±2·18 mg. 17-ketosteroids per g. creatinine (range 8·9–16·0). As no comparison studies have been made on South African Whites and no 17-ketogenic-steroid determinations on the local Bantu, it was decided to determine both 17-ketosteroids and 17-ketogenic steroids in Bantu and local Whites.

Subjects and Methods

The investigation included: (1) a control group of 10 outwardly healthy White women and 10 outwardly healthy White men, aged 22–40; (2) 50 outwardly healthy urban Africans, living in Johannesburg, chosen at random (24 female nurses from the Non-European and Coronation Hospitals and 26 men working at the South African Institute for Medical Research, Johannesburg). Their nutritional state appeared satisfactory. The average age of the Bantu women was 28 (range 22–40) and that of the men 39 (range 20–76); as 6 of the men were aged 50–76 it was decided to place these in a separate group.

Unpreserved accurate twenty-four-hour collections of urine were obtained. Both the 17-ketosteroid and 17-ketogenic steroid values were determined on the same day, the former by the method of Holtorff and Koch (1940), modified by Zimmermann et al. (1952), the latter by the method of Norymberski et al. (1953). To check the accuracy of collection, total creatinine was determined on each twenty-four-hour specimen of urine of the Bantu by the method of Folin (1914).

Results

The findings are shown in the accompanying table.

URINARY 17-KETOSTEROID AND 17-KETOGENIC STEROID VALUES IN OUTWARDLY HEALTHY SUBJECTS

Group	Average volume in 24 hr. (ml.)	Total creatinine (g. per 24 hr.)	17-ketosteroids (mg. per 24 hr.)			17-ketogenic steroids (mg. per 24 hr.)		
			Mean	S.D.	Range	Mean	S.D.	Range
European women	2000		10·5	2·8	6·9–15·6	11·2	2·7	6·1–14·9
Bantu women	1565	1·2	10·5	4·3	5·1–22·2	9·6	4·1	3·6–16·3
European men	1480		12·9	3·9	7·0–21·2	14·7	3·3	10·0–20·7
Bantu men aged 20–49	1892	1·3	15·0	3·7	5·7–16·3	6·8	2·6	2·0–11·1
Bantu men aged 50–76	1836	0·9	10·7	3·7	6·9–15·8	4·0	2·1	2·2–8·2

This table reveals a considerable range of variation in all groups. In both the Bantu and White groups the 17-ketosteroids are very similar. Compared with the 17-ketogenic-steroid values of the Whites, the 17-ketogenic-steroid values in the Bantu women were only slightly decreased, whereas those in the Bantu men were significantly lower. The 17-ketogenic steroids of the Bantu men aged 50–76 were particularly low (between a third and a quarter of the figures for Whites).

Discussion

While urinary excretion of 17-ketosteroids is a measure of testicular and adrenocortical activities, excretion of 17-ketogenic steroids is an index of adrenocortical activity only. Thus, normal 17-ketosteroid excretion in the South African Bantu indicates normal androgenic activity, while low excretion of 17-ketogenic steroids suggests decreased production and excretion of adrenocortical steroids, since the 17-ketogenic steroids are made in the suprarenal cortex only. Allbrook (1956) has found that the average size of the adrenal cortex of East African males is less than that of White Americans. As far as we are aware, the same peculiarity has not been reported among the local Bantu males, but further work on this aspect may be of value.

Summary

Urinary 17-ketosteroid and 17-ketogenic steroid values were determined in 50 outwardly healthy South African Bantu and in 20 Whites.

There was no significant difference in 17-ketosteroid excretion; but excretion of ketogenic steroids was significantly lower in Bantu men. The reason for this is not clear.

We wish to thank Prof. E. H. Cluver for his interest and encouragement, and Dr. P. Keen and Matron E. M. Allen for their cooperation.

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ARMADILLO

A PROTECTIVE CLOTHING AS A SHIELD FROM X-RADIATION

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PROTECTION of the body, and particularly the gonads, against unnecessary radiation during radiography has received increasing attention in the past few years, and many shielding devices have been proposed (e.g., Ardran and Kemp 1957, Abram et al. 1958). None, however, quite met our particular requirement, which was the protection of the gonads of children and adults being X-rayed in the standing position, for studies of the relative content of bone, muscle, and fat in their limbs (Tanner 1955, appendix). Though in these studies the total gonad dose was measured or estimated as only 2–4 milliröntgens, in the case of the children it was to be repeated twice a year for up to ten years, and we felt that even the very small increase in mutation-rate presumed to follow such exposure should be obviated. The same applies, with equal or greater force, to the more usual, and more severe, hospital diagnostic exposures, and to radiographers and physicians as well as to patients.

The only really satisfactory and practical gonad shield seemed to us to be something which could be worn straightforwardly as clothing. We have therefore designed and had manufactured a new material, christened 'Armadillo', which consists of a series of lead scales each sealed in a flexible plastic envelope and imbricated so as to overlap its nextdoor neighbours, both above and below and from side to side, as in Roman armour. Much

Fig. 1—Armadillo protective jockstrap, as normally worn.

Fig. 2—To show practically complete enclosure of scrotal contents by armadillo jockstrap.

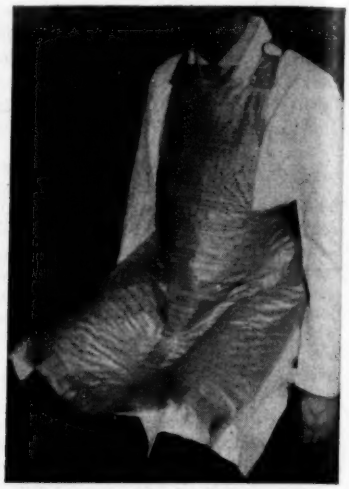

Fig. 5—Full-length armadillo apron, showing the draping qualities which enable it to be shaped over the operator's knees.

flexibility is obtained in this way, combined with all the merits of sheet lead of known thickness; the material can be bent, folded, and shaped to the body contours. It can also be cleaned, or sterilised by autoclaving. The thickness of the lead scales is usually 0·25 mm., but because of the overlap design some 80% of the area is covered by two or more scales, bringing the average lead equivalent thickness (calculated from transmission data at 75 kV) to between 0·3 and 0·4 mm., according to how curved the covered surface is. This is enough to stop 95% of radiation from the kilovoltage range used in diagnosis. The material can be made with scales of other thickness if required.

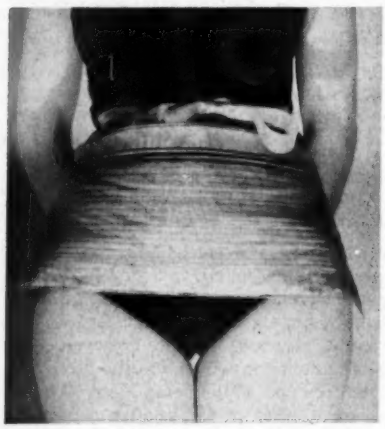

Fig. 3—Armadillo apron for shielding ovaries.

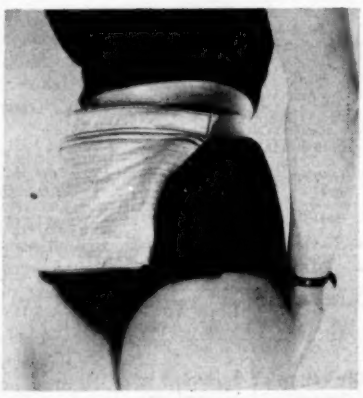

Fig. 4—To show how material may be folded and tucked in as required.

In the female the problem is less completely soluble; we have our subjects wear an apron (fig. 3) measuring 18 in. by 5½ in., which weighs 20 oz. Fig. 4 shows how the material can be tucked up—e.g., for visualisation of a hip-joint.

Fig. 5 shows that a full-length apron can be shaped over the operator's knees—unlike lead-filled rubber aprons. Armadillo aprons are about 30% lighter than lead-rubber ones of equivalent protective power; or alternatively they give that much more protection at the same weight. An additional advantage is that the lead scales can be inspected and seen to be properly placed, whereas in lead-filled rubber or plastic there is little way of knowing whether the lead is evenly dispersed or whether cracking has occurred.

Besides these three items, pads of the material are manufactured for use in protecting any desired part of the body in the lying position. Two sizes are made, one 12 in. × 12 in., the other 12 in. × 30 in., with eyelets at the corners through which weights may be hung, so that the pad can be used at the same time to immobilise and to protect an infant undergoing examination. The possibility of making a garment of this material for protecting the hands is being investigated.

Figs. 1–5 show examples of this material. During the great majority of diagnostic procedures virtually complete gonad protection in the male can be assured if the patient slips on a jockstrap (fig. 1). Placed over the underpants these protectors cause no discomfort whatever; they weigh only 8 oz. and we have ourselves worn them under normal clothes throughout a working day without suffering anything worse than the somewhat quizzical glances of our colleagues.

We had in mind, of course, the protection requirements of the male radiographer. Fig. 2 shows how the jockstrap almost completely covers the scrotal contents, thus shielding them from practically all scatter.

We wish most heartily to thank Mr. R. W. Stanford, of Guy's Hospital, for making measurements of radiation for us and for advising us generally.

The aprons, pads, and jockstraps are manufactured by S. M. Alexander & Co., Bridge Works, Wallace Road, London, N.1, to world patents pending by I. T. Henderson & Co., Ltd. The British distributors of 'Armadillo' are Messrs. Cuthbert Andrews, Bushey, Herts.

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Reviews of Books

Fractures and Dislocations

GEORGE PERKINS, M.C., M.CHIR., F.R.C.S., consulting orthopædic surgeon, St. Thomas's Hospital, London. London: Athlone Press. 1958. Pp. 363. 57*s*. 6*d*.

A PECULIARITY of this book is the absence of any bibliography (indeed, it contains no reference at all to any other published work): this deliberate omission indicates the general pattern of the book—a straightforward account of the personal practice of a very experienced orthopædic surgeon. The examination candidate may look in vain for lengthy evaluations of a variety of treatment methods. But the casualty officer, looking up those methods which are described, will sense the assurance and conviction that derives from first-hand experience.

There are some other novel features—notably, a classification of fractures using stars. "One-star fractures can be safely and competently treated by the patient's own doctor. Two-star fractures are within the province of any doctor who has access to a hospital and an operating theatre". Three-star injuries are reserved for the orthopædic specialist. Such a classification has its merits, but may provoke contention. Few will object to a broken collar-bone being dismissed with a single asterisk, or dispute the claim of a fracture-subluxation of the spine to rank as a three-star catastrophe. But many who specialise in orthopædic surgery have themselves had such unhappy experiences with Monteggia fractures, and with fracture-dislocations of the humerus, that they will feel some surprise (and perhaps relief) that these problems are not earmarked for them.

The procedures Mr. Perkins advocates are an apt blend of the conservative and the operative approach. All his advice on the management of cases bears the happy mark of personal trial. (The child recovering from a fracture at the elbow "is advised to avoid activities that are likely to cause another fall, such as trick-cycling. . . . The advice won't be taken".)

Junior surgeons will welcome the lucid and direct style, and their senior orthopædic colleagues will appreciate the many carefully chosen and beautifully reproduced radiographs. They may, from time to time, wish to dispute with the author some minor item in the text, but such arguments are familiar to orthopædic surgeons.

A Survey of Social Conditions in England and Wales

A. M. CARR-SAUNDERS, D. CARADOG JONES, C. A. MOSER. London: Oxford University Press. 1958. Pp. 302. 25*s*.

THIS book may be regarded as the lineal descendant of one first published in 1927, entitled *A Survey of the Social Structure of England and Wales*. It aims at presenting "a coherent picture of some of the more important aspects of social life in England and Wales so far as they can be illustrated by statistics". The parish is indeed wide, covering many aspects of sociology from fertility to industrial distribution, from health and social security to religion and crime. In the nature of things the book is heavily charged with illustrative statistics; there are over 140 tables, interesting enough in themselves to the statistically minded and presenting in handy form much material of value to the sociologist. But it is more than a mere collection of statistics: it provides a stimulus to thought and many starting-points for discussion.

The chapter on health, after pointing out the improvement in vital statistics and the changing pattern of disease over the past century, goes on to analyse the influence of social class; it shows how the single and the widowed and divorced make a much heavier demand on hospital care than married people and how, with mental as with physical illness, the relatively few patients who stay a long time in hospital account for a high proportion of total bed-occupancy. The authors conclude that many factors must have contributed to the health improvements of recent years, but that much of the credit must certainly go to the National Health Service. "There is scope for many improvements, for greater efficiency all round, more cooperation between doctor and hospital, the creation of health centres and so forth; but a certain amount of inefficiency and waste is a small price to pay for the great benefits in medical prevention and care which the service has brought to the population of this country."

The Theory of Evolution

JOHN MAYNARD SMITH. London: Penguin Books. 1958. Pp. 320. 3*s*. 6*d*.

BOOKS on evolution are numerous, good books are not: this must be quite one of the best, and its appearance in the year of the Darwin centenary is welcome. In spite of its popular format it is remarkably comprehensive, and will prove as useful to the working biologist as to the non-biological inquirer. It is written in the direct and unabstract style to be expected of a pupil and colleague of Prof. J. B. S. Haldane. Reasonable demands are made on the reader's knowledge of biological terms and ideas, but they are not more than can be met by recourse to the Penguin *Dictionary of Biology* and perhaps to an elementary textbook of genetics. Selection, population structure, speciation, the phylogeny of man and animals are all discussed: some of the more recent ideas which we owe to Waddington and to Goldschmidt have proved particularly amenable to Dr. Maynard Smith's use of concrete instances to illustrate principles (not a few professional biologists may understand the concept of "canalisation" really clearly for the first time after reading him).

For the doctor a knowledge of human biology is an increasingly necessary prophylactic against public and private errors in matters of genetics, evolution, and the like. Not every medical student need acquire all the knowledge Dr. Maynard Smith provides, but all would benefit from being equipped with the ideas he outlines. It is only at the end of the book that the author allows himself to speculate directly on the most interesting of problems in human biology—the evolution of human society, and of long childhood, complex psychosexual development, and second-order "heredity" through cultural transmission of information which distinguish man. This discussion is all too short, on the psychological side in particular.

In man elements which are phylogenetically sexual and reproductive appear long before maturity and seem to have evolved an important function in character formation. The relation of this process to the abnormal length of childhood, by mammalian standards, is a fascinating biological question. Dr. Maynard Smith here follows Malinowski rather than Róheim in stressing culture above phylogeny, thereby leaving another book to be written in the future. The account of his own work on the courtship of flies, where the female rejects any male unable to keep up with her in an athletic dance, and in which hybrid males were found to perform more successfully than inbreds, makes fascinating reading.

Thudichum: Chemist of the Brain

DAVID L. DRABKIN, professor of biochemistry, Graduate School of Medicine, University of Pennsylvania. Philadelphia: University of Pennsylvania Press. London: Oxford University Press. 1958. Pp. 309. 40*s*.

MOST doctors are familiar with a nasal speculum which is fashioned from a single strip of metal, bent to resemble a pair of sugar tongs, but with its ends shaped to fit into the nostril. Many will know that such an instrument is properly called Thudichum's speculum. But how many know who Thudichum was, or realise that he held a chair, not of otorhinolaryngology or even of surgery, but of chemical pathology at a London hospital?

His claim to fame does not, of course, depend upon the invention of this instrument. (That was an incident in a period when he worked as a general practitioner, and developed a flair for removing nasal polyps.) He was, Professor Drabkin contends, "the greatest chemist between Justus von Liebig and Emil Fischer", and a "genius neglected by his own century"; and those are the grounds which have prompted

him to prepare this, the only biography of Thudichum yet written.

All who read this book will agree that such a full-length study was long overdue, and that Thudichum's career was one that provides a rich subject for any author—not only because he was a pioneer in biochemistry (he made fundamental contributions to our knowledge of urinary and biliary pigments, applied the technique of spectro-analysis to the examination of these materials, and isolated such substances as cephalin and sphingomyelin, for the first time, from brain tissue); but also because of the multiplicity of his interests (he wrote books on cooking and on the culture of vines, and built what was possibly London's first Turkish bath).

Though he died only fifty-seven years ago, the details of his life have not been easy to determine, and some of the most interesting pages in this very interesting book are those describing the research which went into its production.

Humanistic Psychology

JOHN COHEN, M.A., PH.D., professor of psychology, University of Manchester. London: Allen & Unwin. 1958. Pp. 206. 18*s*.

THERE is something about psychology that makes its students take one of two opposite directions: some seek to see the human mind in all its glory and try to examine and collate its varied and impressive manifestations; others can make nothing of all this and prefer to examine in minute and strictly scientific detail some small aspect of, for example, the stimulus-response law. Professor Cohen is in the first division and paints extravagantly on the broad human canvas: aiming as he does, at a public varying from general readers through psychologists, psychiatrists, and sociologists to philosophers, his picture becomes a little misty at the edges. He quotes from such sources as Euripides, Ecclesiasticus, and Edward the Confessor; and he quotes so often that some readers may begin to feel lost.

His main thesis, however, is well worth arguing—namely, that man is something special and what rats do in mazes probably does not tell us very much about the human being. He believes too that the qualities of human experience transcend the activities of the central nervous system. He is often entertaining, especially at the expense of other psychologists, and he has a few good things to say about the growing child. He also tackles sensation, time-perception, the origins of thought and work, and psychological aspects of illness and literature.

General Diagnosis and Therapy of Skin Diseases

H. W. SIEMENS, M.D., professor of skin and venereal diseases, University of Leiden, Holland. Translated from the German by KURT WIENER, M.D. Chicago: University of Chicago Press. London: Cambridge University Press. 1958. Pp. 324. 75*s*.

THIS book was written because the author felt that a new approach was necessary in the teaching of dermatology. Many will agree, but they may be disappointed in how far the book has achieved it. The first part is devoted to the painstaking recognition of cutaneous physical signs which is the basis of the diagnosis of skin disorders. It is done exceedingly well, but it is on entirely traditional lines and is the sort of thing that any teacher attempts in the clinical instruction of students. The fluency of the text is hampered by too much of the fussy latinity that students mistake for the real stuff of dermatology, and the translation is at times slavish. This part is profusely illustrated with black-and-white photographs most of which are very helpful, but they cannot depict the nuances of hue that are often as important as other physical features.

The second part discusses local treatment in detail of greater interest and significance to those who have tried the treatment than to students fresh to the subject. Professor Siemens is well known for his critical studies in this empirical field, and it is useful to have his views collected together. Again, much of his material is not novel and there are few references to modern bases and active medicaments. Most undergraduates have their interest in dermatology maintained only by learning about diseases, and they are unlikely to enjoy a book where the natural history of the things they see is deliberately omitted. Postgraduate students, however, will profit from the standards of exactness that it encourages.

Chronic Schizophrenia

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THIS is not a treatise on chronic schizophrenia, but a psychoanalytically coloured account of the psychopathology of this condition, and of an experiment in which mental nurses were given better opportunities than previously of forming durable relationships with schizophrenic patients in a treatment unit. The patients had been in "chronic refractory wards", and were of both sexes: they had been treated, without lasting benefit, by insulin coma and electroconvulsion therapy. The nurses, who at the outset of the experiment had evidently little understanding of what was going on in these patients, were encouraged to discuss freely the abnormal behaviour they observed, so that its significance could be explained; thereby they became more confident and secure in their dealings with the patients. The authors do not present their results in detail, but it is clear that they were gratifying. No attempt is made to relate them to the excellent results reported by other observers, from Klaesi onwards, using apparently different methods.

Lectures on the Scientific Basis of Medicine

Vol. VI, 1956–57. London: Athlone Press. 1958. Pp. 393. 45*s*.

THE British Postgraduate Medical Federation continues its successful series of lectures, and those of the sixth winter are now brought together. No physician who values his own cultural background should miss the opportunity of consulting and reading in these important volumes. The variety of topics range from the opening address by Sir John Cockcroft on the biological significance of atomic energy, through new technical surgical matters such as arterial substitutes, homotransplantation, and heart-lung machines, to brain and neuromuscular biochemistry and physiology. The general reader will be attracted by the account of Cajal and Sherrington by Prof. E. Liddell and a lecture on social psychiatry by Prof. Aubrey Lewis, which is a masterpiece of erudition and trenchant critical commentary. Dr. Mary Barber deals with the problem of resistant staphylococci, to which she first drew attention some ten years ago and which is one of the major practical problems today in our hospitals. This volume is a worthy addition to a series which has made a creditable display of fundamental medical research in Britain.

Recent Advances in Oto-Laryngology (3rd ed. London: J. & A. Churchill. 1958. Pp. 438. 60s.).—The new edition of this book, now edited by Mr. Boyes Korkis, lives up to its title, for it contains many up-to-date ideas and operative techniques which will be of great value to the postgraduate student. It is perhaps in otology that the most interesting changes are found; the accent is on improvement in hearing both by operation and by the use of aids. The book includes a helpful description of stapes mobilisation for otosclerosis and tympanoplasty, which, because of the chances of maintaining hearing in middle-ear disease, will surely be increasingly used, in one of its modifications, rather than simple mastoidectomy. The day seems to have arrived when a binocular microscope is a must for the kit of the aural surgeon. Apart from several interesting chapters on the ear, with consideration of both cochlear and labyrinthine functions, this edition also deals with the most recent treatment of malignant lesions of the nose, palate, and larynx, facial palsy, and lesions of the œsophagus. The place of cortisone in the treatment of facial palsy and œsophageal lesions is assessed: much help seems to have been gained from its use at the right time.

THE LANCET

LONDON 11 OCTOBER 1958

The Rising Crime Wave

THE *Criminal Statistics* for 1957 [1] suggest that the amount of crime in England and Wales is increasing, and indeed according to these Home Office figures the general picture for the year is gloomy. They suggest that serious offences of all types are on the increase; and, on the face of it, it looks as though the community were much more criminally disposed than in pre-war days.

The total number of indictable offences known to the police for 1957 was 545,562—an increase of 21,000 on 1951, which has hitherto been regarded as the peak year for known crime. More breaking and entering offences, more robberies, more crimes against the person, more sexual offences, were recorded. The number of homicides remained more or less constant at 142, as against 145 in 1956; but, owing to changes due to the operation of the new Homicide Act in 1957, exact comparison with previous years is difficult.

Certainly the figures for 1957 prove that the number of serious crimes known to the police has risen, that teenagers are responsible for a large part of the increase, and that young men have been the most generous contributors to these statistics (the annual increase for those found guilty of indictable offences being 23%). But we must not assume that an increase in crimes known to the police necessarily signifies an increase in criminal activity in the country. The association between these two follows no straightforward mathematical law. Homicide, for instance, is notoriously difficult to conceal, and the number of offences known to the police probably approximates to the number committed. (It is perhaps worth noting that, in this category at least, 1957 is no worse than preceding years.) Sexual offences, on the other hand, are difficult to discover, and a rise in the number of these offences known to the police might be due to greater vigilance. Indeed the actual number of such offences could decline, though the number known to the authorities showed a sharp increase. Amid this welter of statistics there is precious little firm ground on which to base either assured judgments or casual theories. As Lord PAKENHAM has pointed out,[2] these official returns show an "appalling incapacity . . . to reveal the true state of crime in the country . . . and there is no kind of disposition to give them the same sort of credence as we give to those, shall we say, produced by the Treasury, the Board of Trade, or other . . . departments for their various purposes".

If it is true that official figures can be so misleading, can any reliance be placed on them, and can any even tentative conclusions be drawn from them? In view of the uncertainty of the experts the answer must be: probably not. A rise in the annual figures is no more to be viewed with sudden alarm than a decrease should be made the ground for complacency. But we should accept them as evidence that there is a fair amount of crime in this country (certainly more than the figures reveal and much more than we would like to believe), that males are more criminally disposed than females, and that young males are disproportionately active delinquents.

The number of children and young people under 21 who commit known offences year after year shows that our society has a serious juvenile problem. But whether in 1957 there was more or less misbehaviour among young people is really a side issue. Our real concern should be with the fact that so many indictable offences are committed, not by professional criminals, acknowledged outlaws preying upon an innocent population, but by apparently ordinary members of society who either cannot or will not accept its legal norms. As a community we must ask ourselves why this is. What factors in our social structure predispose so many youngsters to illegal activities? What are the forces at work in what, for want of a better term, we may call the youth culture-pattern (especially in big towns) which make for delinquency and perpetuate forbidden deeds as traditional modes of behaviour, or misbehaviour? These questions raise tremendous issues that will not be resolved by vague generalities about the decay of family life, the decline in morals, and poor church attendance.

The public and their administrative and political leaders have not yet grasped two simple and salient facts. The first of these is that crime is too wide and nebulous to have a single cause. As Lady WOOTTON OF ABINGER wrote recently [3]: "One might as well look for some equally simple 'cause' to account for the presence in Piccadilly of all the people who happen to be there at any particular moment." Within the general body of known and unknown offenders are different types of people, following different patterns of life, who tend to commit special sorts of offences. Criminology will make little progress until it studies these types of people and their patterns of behaviour. The second salient fact that is generally overlooked is that as a community we do little about prevention. Even with our present knowledge, much useful experimental work could be done using the slender clues we possess. Instead of deploying forces comparable to those we have turned against other social evils, such as poverty or ill health, we grudgingly provide money to build a few new prisons, and to back such desperate gambles as detention centres. Hardly a penny can be found for preventive services or for the research projects which should underpin such schemes. The greatest single need is for operational research units whose task it would be, not to seek out the probably indefinable causes of crime, but to develop techniques for handling particular types of offenders, not necessarily in special institutions but as far as possible within the framework of their present social background. Until this is done the annual criminal statistics are not going to fall permanently to a level at which all honest citizens can have an easy conscience.

1. Criminal Statistics, England and Wales. 1958. H.M. Stationery Office. Cmnd. 529. Pp. 94. 8s.
2. Address to the Magistrates' Association, 1955.
3. *Observer*, May 18, 1958.

Experimental Shock

IT has long been recognised that some types of extensive soft-tissue injury are apparently beyond the scope of surgical technique and almost invariably cause death despite energetic and even heroic treatment. Large lacerations of the muscles of the thigh and buttocks with extensive crushing of the pelvis are perhaps the commonest of such injuries; and even when adequate early treatment of the injuries with apparently good control of bleeding and full replacement of blood-loss by transfusion are possible, irreversible shock usually leads to death. The experience of many surgeons in the 1914–18 and 1939–45 wars and more recently in Korea was that few patients survive such injuries. It is greatly to the credit of OCHSNER and his colleagues that without the immediate stimulus of war they have devised a means of producing a severe experimental injury of this kind in both hind limbs of Texan goats in circumstances which have enabled them to discover much new evidence.[1–4]

They found that in Texan goats the initial external blood-loss, provided it did not exceed 15 ml. per kg. body-weight, was unrelated to the duration of survival, but there was a very large range of initial as well as total external blood-loss. It was not possible to measure intramuscular bleeding and to decide whether early death was related to an unusually large loss of blood into the injured tissues. The initial hæmoglobin level before wounding also was unrelated to survival-time. Loose dressings were no better than none at all, but pressure-dressings increased mean survival-time from 18·9 to 24·7 hours; even incomplete aseptic precautions also prolonged survival. The old belief that movement, and especially rolling, is bad for the shocked patient is supported by the reduction in survival-time which followed turning over the goats once every four hours after injury; most of the animals died shortly after one of these changes of position. Survival was also reduced by interference and manipulations which were necessary for the making of experimental observations—which accords with the experience of some observers of severe shock in injured men.

Replacement of the total measured blood-loss with blood, with blood and dextran, or with dextran alone showed that survival-time was nearly doubled when 1500–2000 ml. of blood in excess of the measured loss was given, was increased by 500 ml. blood or by dextran and blood, but was reduced by dextran alone. When penicillin was injected alone or in combination with dihydrostreptomycin, or when aureomycin or chloramphenicol was injected intravenously, survival-time was increased, more than by blood-transfusion, provided there was no delay between the infliction of injury and the beginning of treatment with the antibiotic. The combination of penicillin with transfusion of at least 1000 ml. more blood than was lost externally increased survival-time more than either agent alone, but no animal survived when treated by transfusion of whole blood even when this was combined with antibiotic therapy. The only surgical treatment that resulted in survival was bilateral disarticulation at the hip-joints; but, when transfusion and antibiotic therapy were started immediately after injury, surgical treatment could be delayed for up to twenty-four hours provided the wounds were cooled with ice; without local cooling survival depended on surgical treatment being done within four hours of injury. OCHSNER et al. concluded that the need to amputate early in the absence of local cooling, despite adequate transfusion of whole blood and antibiotic therapy, suggested that some toxic factor may be liberated in the injured tissues; but the possibility remains that continued oozing of blood into the injured tissues may be at least as important a lethal factor.

MANSBERGER et al.[2] believe that the protective effect of antibiotics is probably due to direct suppression of bacterial growth in injured tissue, which under the conditions of their survival experiments became heavily infected with a mixture of organisms. JACOB et al.[5] emphasised the importance of bacterial infection as a factor in the development of irreversible shock in laboratory animals, but were unable to identify the mode of this bacterial activity. In the preparation of OCHSNER et al., the reduction of the fæcal bacterial content by oral administration of antibiotics did not prolong survival unless the drug was absorbed into the blood-stream. Attempts to reduce local infection by irrigation of the wounds with tap-water, 0·9% saline solution, or 3% hydrogen-peroxide solution, or by packing with 3% zinc-peroxide paste, only slightly increased survival-time, whereas the local application of ice alone prolonged survival by about 50% and prevented gross muscle necrosis and the development of a pungent odour in the wounds. The local application of either penicillin or aureomycin prolonged survival-time, but neomycin did not have any effect. The most effective local application was the combination of penicillin and ice; which MANSBERGER et al.[3] think may indicate that, besides inhibition of bacterial growth, there is some interference with the absorption of bacterial toxin. They did not find any consistent evidence of bacteræmia in their untreated animals, and this justifies their conclusion that if a bacterial factor is important in the development of irreversible shock it is likely to be one confined to the damaged tissue. In support of this, in further experiments they showed that in animals treated with penicillin the inhibitory effect of the drug on bacterial growth was greatest during the first six hours after wounding; after eighteen hours the concentration of bacteria in muscle was as high as in the untreated controls; but the organisms had penetrated only 2–3 cm. from the lacerated surface of the muscle, although there was structural damage at a greater depth than this. The early effect of penicillin was greatest on gram-positive organisms, but there was also a reduction in the content of gram-negative organisms either directly or because of

1. Ochsner, E. W. A., Jacob, S. W., Mansberger, A. R. *Surgery*, 1958, **43**, 703.
2. Mansberger, A. R., Ochsner, E. W. A., Jacob, S., Oppenheimer, J. H., Gillette, R. W. *ibid.* p. 708.
3. Mansberger, A. R., Oppenheimer, J. H., Gillette, R. W. *ibid.* p. 721.
4. Oppenheimer, J. H., Knecht, A. T., Mansberger, A. R., Gillette, R. W., Pon, R. S. *ibid.* p. 730.
5. Jacob, S., Weizel, H., Gordon, W., Korman, N., Schweinburg, F., Fine, J. *Amer. J. Physiol.* 1954, **79**, 523.

the suppression of the gram-positive organisms. It is noteworthy that streptomycin did not prolong survival-time. Since one injection of penicillin immediately after the injury prolongs survival, but injection twelve hours after injury is associated with as short a survival-time as in the untreated controls, the bacterial factor appears to develop and act soon after injury.

These observations are clearly of great importance in the treatment of severe injuries. They do not in any way alter the well-established general principles of adequate excision of all dead and damaged tissue, if necessary by amputation, and of complete replacement of lost blood by transfusion. OCHSNER et al. suggest, however, that when many people are injured and hospitals and surgical teams cannot deal with them, the combination of local and systemic administration of penicillin or aureomycin with local cooling of the wounds by packing them with ice and the application of a tourniquet just above the injury on mangled limbs may prolong survival of both patient and limb. Their work is an important attempt to find out more about one of the most puzzling aspects of very severe injury.

Banting Up to Date

FOR most of us the name of BANTING will always be associated with the discovery of insulin in 1922. The name, however, had passed into the language [1] half a century earlier for a very different reason. WILLIAM BANTING, a London undertaker, was so pleased with the response of his obesity to a new dietary regimen that he published his famous *Letter on Corpulence* [2] in 1863, having first rejected the idea of writing to *The Lancet*. Although GRAHAM [3] refers to the " well-known Banting cure ", it is probable that few nowadays have much idea of the diet BANTING described. Two small volumes on obesity [4 5] have recently appeared, which though intended for the layman, raise several matters of interest and importance to his doctor. Both offer advice with many points in common, and both recall some features of the diet eulogised by BANTING.

YUDKIN [5] takes the view that obesity is associated with an excess of energy intake over output. Differences in energy output between individuals may be considerable, but he emphasises how the energy balance is rigidly maintained in most of us by the hypothalamic centres regulating appetite. The implication is that the amount of exercise many people fail to take may well be important for more reasons than the reduced expenditure of energy involved. YUDKIN recalls the work of MAYER et al.[6] who demonstrated how the restricted exercise of sedentary but well-fed workers appeared to disorganise the mechanism normally responsible for equating food intake with energy output. They were able to show that when energy output is much reduced and there is free access to food, more is eaten than the amount required to maintain energy equilibrium on a regimen providing more exercise. In these circumstances, it is not surprising that fat accumulates; restriction of physical activity may well be a more important cause of obesity than is generally believed. PASSMORE [7] has now confirmed in the dog the important relation between exercise, appetite, and weight, which MAYER and his colleagues [8] had described earlier in rats. Other studies in children [9 10] and in adults [11] all tend to confirm that when exercise is much reduced and there is free access to food, energy requirements tend to be exceeded and weight inevitably increases. In this connection, the importance of another factor in energy economy is recalled by the work of BOOYENS and MCCANCE,[12] who recently investigated the striking variations in energy expenditure of healthy men and women. They found 3 among their 36 normal subjects with metabolic-rates as much as 30% below the average for the group. Yet none of these was overweight, and each had obviously managed to maintain his energy equilibrium in spite of low requirements.

YUDKIN goes on to describe how the carbohydrate of cereals has come to form so important and often excessive a proportion of man's diet, and he believes that the failure to reduce carbohydrate, when an adequate supply of protein and fat is available, is a fundamental fault of the diet of civilisation. He takes particular exception to the large amount of sugar consumed in Britain today; sugar consumption has increased fivefold over the past century. For these and other reasons, he advises a reducing diet with the emphasis on restriction of carbohydrate. Reduction in the intake of fat will inevitably follow, and in this way calorie intake will be limited sufficiently for weight reduction to occur.

The Banting episode and the controversy it aroused are described by MACKARNESS,[4] and he uses the story as the background for a discussion of some of the recent work on obesity by KEKWICK and PAWAN [13] at the Middlesex Hospital. BANTING's dietary regimen, which was based on advice given to him by an aural surgeon named WILLIAM HARVEY, may have provided as many as 2800 calories daily, much of it in the form of protein. On this system he claimed to have lost 46 lb. in a year, without restrictions as to quantity and on " a dietary table far superior to the former "—namely, his usual diet. The regimen was primarily designed to exclude carbohydrate as far as possible, though the fat content was also restricted. It included " 2 or 3 glasses of good claret, sherry or Madeira " for dinner and " a glass or two of claret " with supper, as well as a tumbler of grog for a nightcap if required. BANTING believed, as he had been told, that foodstuffs containing starch were responsible for the accumulation of fat by the obese, and that stringent restriction of such items in his diet had solved the problem of adjusting his weight. KEKWICK and PAWAN [13] have shown that when patients

1. Concise Oxford Dictionary. London, 1946.
2. Banting, W. Letter on Corpulence. London, 1863.
3. Graham, G. *in* A Textbook of the Practice of Medicine; p. 502. Edited by F. W. Price. London, 1950.
4. Eat Fat and Grow Slim. By RICHARD MACKARNESS, M.B. London: Harvill Press. 1958. Pp. 128. 10*s*. 6*d*.
5. This Slimming Business. By JOHN YUDKIN, M.A., M.D., PH.D., M.R.C.P., F.R.I.C. London: Macgibbon & Kee. 1958. Pp. 191. 15*s*.
6. Mayer, J., Roy, P., Mitra, K. P. *Amer. J. clin. Nutr.* 1956, **4**, 169.
7. Passmore, R. *Lancet*, 1958, i, 29.
8. Mayer, J., Marshall, N. B., Vitale, J. J., Christensen, J. H., Mashayekhi, M. B., Stare, F. J. *Amer. J. Physiol.* 1954, **177**, 544.
9. Bruch, H. *Amer. J. Dis. Child.* 1940, **60**, 1082.
10. Johnson, M. L., Burke, B. S., Mayer, J. *Amer. J. clin. Nutr.* 1956, **4**, 37.
11. Dorris, R. J., Stunkard, A. J. *Amer. J. med. Sci.* 1957, **233**, 622.
12. Booyens, J., McCance, R. A. *Lancet*, 1957, i, 225.
13. Kekwick, A., Pawan, G. L. S. *ibid.* 1956, ii, 155.

are given diets providing the same number of calories from sources predominantly fat, protein, and carbohydrate respectively, they lose weight most rapidly if the diet consists largely of fat, less rapidly with protein, and least of all on carbohydrate. Indeed, weight gain was sometimes recorded with the third type of diet. Although changes in the diet were not associated with any remarkable alteration in the basal metabolic-rate, they suggested that "the rate of katabolism of body fat may alter in response to changes in the composition of the diet"; in support of this, they cited the increased loss of insensible water on high-fat and high-protein diets, compared with the reduced loss on high-carbohydrate diets. WERNER [14] has also compared the effect of high-fat and isocaloric high-carbohydrate diets on weight-loss; he concluded that the slight differences demonstrated in 4 only of his 6 patients could readily be accounted for by variations in salt and water balance.

The meaning of KEKWICK and PAWAN's [13] findings may be obscured unless the close relation between water metabolism and fat consumption is borne in mind. HOLT [15] recalls that pædiatricians are familiar with the reversible loss of weight which infants undergo when transferred from a high-carbohydrate to a high-fat diet and vice versa, and he attributes this to changes in body-water content. In 1907, BENEDICT and MILNER [16] described a subject under strict supervision in a calorimeter chamber, who when changed from a high-carbohydrate to a high-fat diet lost 2·7 kg. of body-weight in three days, although in energy balance. In a recent study of 7 fat patients, PASSMORE et al.[17 18] calculated that with daily energy deficits of approximately 2500–3000 calories, large quantities of tissue fat were being metabolised. Each of these patients lost as much as 2–4 litres of body-water during the first week, in contrast to the much smaller losses, or even retention, of water found during the subsequent five weeks on the same regimen. KEKWICK and PAWAN's observations were usually limited to periods of five to nine days on a single dietary regimen, and it would be wrong to assume that the striking losses of weight they found in some of these brief periods would continue at the same rate if the dietary regimen were prolonged.

CHALMERS et al.[19] have now found that modifications in the diet of obese patients may be associated with changes in the excretion of "fat-mobilising activity" in the urine, and that this activity is greatest in the urine of normal subjects when fasting, and of obese patients on a diet composed of 90% fat or protein, while it disappeared on a diet of 90% carbohydrate. Further evidence will be awaited with interest on the relation of this activity to the lipid-mobilising peptide in blood described by SEIFTER and BAEDER [20] and to another substance in blood associated with fat-transport activity, recently described by REITH and THOMAS.[21]

14. Werner, S. C. *New Engl. J. Med.* 1955, **252**, 661.
15. Holt, L. E. *J. Amer. med. Ass.* 1957, **164**, 1890.
16. Benedict, F. G., Milner, R. D. *Bull. U.S. Off. Exp. Stas*, 1907, no. 175.
17. Passmore, R., Strong, J. A., Ritchie, F. J. *Brit. J. Nutr.* 1958, **12**, 113.
18. Strong, J. A., Passmore, R., Ritchie, F. J. *ibid.* p. 105.
19. Chalmers, T. M., Kekwick, A., Pawan, G. L. S., Smith, I. *Lancet*, 1958, i, 866.
20. Seifter, J., Baeder, D. H. *Proc. Soc. exp. Biol., N.Y.* 1957, **95**, 469.
21. Reith, W. S., Thomas, M. J. *Nature, Lond.* 1958, **182**, 604.

Both YUDKIN and MACKARNESS recommend low-carbohydrate diets with abundant protein. YUDKIN considers that the fat intake will then adjust itself; MACKARNESS, basing his argument on KEKWICK and PAWAN's short-term experimental results, urges the importance of increasing the intake of fat. The criticism that diets consisting largely of protein and fat will prove more costly than many patients can afford is anticipated and answered effectively, certainly for those who are likely to read these two books. In view of the tendency today to associate myocardial infarction with cholesterol metabolism, and this in turn with dietary fat, any regimen which seeks to increase the fat intake is bound to arouse misgivings. This question was discussed last year by YUDKIN,[22] and he concluded that it was "difficult to support any theory which supposes a single or major dietary cause of coronary thrombosis". He added that "relative overconsumption of food, associated with reduced physical exercise, may be one of several causes of the disease"—just indeed the conditions which create obesity. The size of the problem posed by obesity may be obscured to some extent by its very familiarity. Any effective and practicable system proposed for its solution will depend for its success on placing the responsibility for its execution where it belongs—on the shoulders of the patient. For this purpose, the greatest need is to enlighten the patient, and both YUDKIN and MACKARNESS have provided palatable and even entertaining statements of the problem, garnished with appropriate advice. Both will appeal to some of the patients for whom they were designed.

Annotations

THE AFFAIR AT BATH (CONTINUED)

LIKE proposals to abolish or amalgamate old regiments, proposals to abolish or amalgamate old hospitals are apt to cause a sharp reaction. The reason is that a hospital, like a regiment, is something into which many people have put their hearts, and to which they are irrationally devoted. Planning of hospital services, like modernisation of the Army, is a necessity, and the view of the planners must be wide. But scope must still be found for the people with a narrower and more intense vision of what they want for their particular town or for the group of patients they are treating. Planners are properly concerned with keeping things in proportion; but it is usually enthusiasts, who see things out of proportion, that make progress and set new standards. In the old days they could fire others with their purpose and thus raise money for a department or hospital; and Sir Harry Platt is not alone in thinking that, since our Governments are unlikely to find enough capital for the National Health Service, this custom will have to be restored.[23]

The affair of the Royal National Hospital for Rheumatic Diseases at Bath was, we thought, a case in which the planning authorities in the Ministry of Health and the region did not attach enough importance to exceptional conditions.[24] Founded in 1742, the hospital

22. Yudkin, J. *Lancet*, 1957, ii, 155.
23. See *Lancet*, 1958, i, 1270. Russell, W. R. *ibid.* 1957, ii, 188.
24. *ibid.* 1957, i, 1028.

had a reputation sufficient to justify the word " national " in the title it took in 1934. During the war it was badly bombed; but when peace returned, no repairs were done, because it was to have a new building for which the City of Bath had given a site. In 1948, when the National Health Service absorbed its endowment fund of £130,000 (including £89,000 specifically given for rebuilding), nobody doubted that the plan would go forward, but, in relation to other needs, the regional board later assigned low priority to this project. The Ministry, for its part, refused aid because it felt that, though more than half the patients came from outside the region, the regional priorities were for the board to decide. Presumably the Ministry felt, too, that the treatment of rheumatic diseases could now be as satisfactorily undertaken at general hospitals, and that there was no longer any need to preserve and develop, nationally, a special centre for the purpose. For our part, however, we thought that the arguments were still strongly in favour of having such a centre; and we are therefore glad to know that when, eventually, the regional board set up a subcommittee to go into the whole question of the care of rheumatism in the region, this committee reported unanimously in favour of the rebuilding of the hospital at Bath.

For those who believe in the hospital and its potential value, the situation is now more hopeful. The Ministry sticks to its view that the regional board must find the money, but it may be prepared to help if the board puts up a strong case. Neither board nor Ministry, it seems, is exactly anxious to find, even over five years, the £250,000 now required; and no doubt they have many other things they would like to do with it—things that may be even more pressing. But to the outsider it must still seem that £250,000 is a great deal less in value than the £130,000 which the N.H.S. acquired from the hospital in 1948; and granted that the hospital is to be continued at all, the revised scheme, though hopeful, is far from extravagant.

Installation of a lift shaft (beginning this month) will be followed by rebuilding of the war-damaged wing and then by reconditioning of the other block. The new plan will house the nurses (at present in hired accommodation) and allows for the incorporation in the hospital of the research unit, on which its special value will so largely in the end depend.

The Clinical Research Board and the Medical Research Council have accepted responsibility for the research unit, and have appointed an advisory committee consisting of professors of Bristol University and clinicians on the staff of the hospital. But, though the Clinical Research Board and the M.R.C., according to their normal practice, would pay for salaries, the rooms in which the work is done will have to be provided by the regional board or the Ministry. To have the unit anywhere but in the hospital building would be to start off, once more, on the wrong foot.

Meanwhile some useful help in another way may be given by the British Rheumatic Association. Though most of the old Pump Room Hotel is to be pulled down and rebuilt as flats and shops, the hospital's treatment centre for outpatients will remain in it, and the Association is thinking of taking over two floors above this for use as a partly subsidised hostel for the patients having treatment.

With everyone now determined to make it a success, the present compromise should turn out well, and the Royal National Hospital for Rheumatic Diseases, as a specialist hospital for arthritis, will have its chance of showing in which ways it can improve on the care given at general hospitals and can advance knowledge. We are left, however, with the larger problem of discovering how, in an organised service, anybody can get such a chance if he wants it enough. Too often in these early years the N.H.S., intent on discharging its large responsibilities in a big way, has discouraged individual and local enterprise, as certainly happened at Bath. If Sir Harry Platt is right, we may yet have to rely on such enterprise for much of the hospital development which is now becoming so obviously necessary.

A DOMESTIC DELILAH

A REMEDY for alopecia in the Ebers papyrus includes the fat of the hippopotamus—a curiously bald beast to choose as a source of pilary stimulation. Centuries of medical advance have added few hair restorers of more certain value. In the scalp clinic of a dermatological Mecca used to be heard the rhythmical exhortation " *tous les soirs vous allez faire une friction* " with, amongst other things, carbon disulphide. Where doctors fail, trichologists flourish. In quiet moments undisturbed by the clink of coin, these experts can be induced to confess that their expensive secret consists in no more than stopping their clients from inflicting physical or chemical violence on their scalps.

Mothers are familiar with the temporary patch of baldness on the back of a baby's head when, active but not yet sessile, the child rubs its head on the bed. A few older miscreants are known to pull out their hair, sometimes swallowing the evidence. Adolescent girls smitten by the equine folly wear their hair in " pony tails ", which tends to drag the hair out at the temples. This form of baldness is endemic in Greenland, where this style is traditional.[1] It was not uncommon when curlers and felt slippers were de rigueur in the bistros of Camden Town. Zealous massage or friction is often resorted to by the balding, usually on the advice of barbers or doctors, and this may aggravate the baldness by twisting and breaking the hair.[2] Overindulgence in bleaching and chemical waving makes the hair fragile, and loss of hair is seen in American Negro women who paradoxically want to make their hair straight.

A new source of traumatic alopecia has been described by a doctor with special experience in the disorders of the scalp and hair. Dr. Agnes Savill [3] reports that patients of each sex and various ages came to her complaining of loss of hair, yet showing no disease to account for it. All had been using hair-brushes containing bristles made of nylon instead of the old-fashioned hog bristles. In some of their brushes, hairs could be seen that had been pulled out at the roots, while others had been broken off and were split longitudinally. It is not surprising that nylon should be brutal to the hair. It is hard and makes indestructible pot-scourers. Some dentists have deplored the use of nylon toothbrushes, and professional footballers have protested against nylon studs as these inflict nasty injuries. Dr. Savill also blames the shape of the ends of the bristles, which when they are cut off square seem harsher than when they are rounded.

Clearly there must be special reasons why some people are affected when the majority presumably are not. Her patients did not have any abnormality of the hair which predisposed them to this type of damage, and they all

1. Hjorth, N. *Brit. J. Derm.* 1957, **69**, 319.
2. Bowers, R. E. *ibid.* 1950, **62**, 262.
3. Savill, A. *ibid.* 1958, **70**, 296.

recovered without treatment when they stopped using the nylon brushes. Apart from square-ended bristles, some brushes may have some feature of design which makes them unsuitable, or possibly the force with which they are used matters more than with brushes that have softer bristles.

THE TREATMENT OF GONORRHŒA

A BACTERIOLOGIST who has spent much of his working life dealing with the gonococcus recently stated that he thought it was a neglected organism of which we still knew very little.[1] This may seem a surprising assertion concerning an organism which was discovered nearly eighty years ago and is known to be a major cause of human suffering. Nevertheless it is correct, and our ignorance about it is reflected in the uncertainty which surrounds the future of the treatment of gonorrhœa.

Up to the late 1930s there was no specific remedy, and treatment consisted in encouraging the natural immunity of the patient and establishing drainage when necessary. The introduction of sulphonamides marked a new era; the organism appeared highly susceptible, and complete conquest of the disease was confidently predicted. Despite the sulphonamides, the incidence of the disease increased enormously in the 1939–45 war, and in the early 1940s it began to be evident that some strains of gonococci were becoming sulphonamide-resistant. At first, relatively few patients failed to respond to treatment; but when the armies of North Africa invaded the Italian peninsula in 1943, resistant cases suddenly increased alarmingly,[2] and it soon became clear that the remedy had lost its efficacy.

The immediate problem was solved by the arrival of penicillin, to which the gonococcus proved highly susceptible. Symptoms and signs were abolished within hours by very small doses of penicillin; resistance to treatment was quite uncommon, and was soon overcome by larger but still moderate doses of the drug. The incidence of venereal diseases reached its peak after the war was over and thereafter declined sharply, the start of the decline coinciding with increasing supplies of penicillin. The solution of a serious problem seemed to be at hand. The incidence of gonorrhœa continued to decline until 1955, when for the first time since the war the annual report of the chief medical officer of the Ministry of Health [3] indicated an increase in the number of patients with gonorrhœa attending the clinics. The rise in incidence has continued and has accelerated.[4]

It seems that several factors are concerned in this increase; but one, and possibly the most important, is the emergence of penicillin-resistant strains of gonococci. At the end of 1956 Curtis and Wilkinson [5] noticed that a small proportion of men with uncomplicated gonococcal urethritis who attended a large clinic for venereal diseases in London failed to respond to the routine treatment of 300,000 units of procaine penicillin given intramuscularly; and their discharges continued to contain gonococci. In some of these cases further treatment with larger doses of penicillin was equally unsuccessful. Between November, 1956, and December, 1957, 1267 cases of acute gonorrhœa in men were seen, of which 1116 were treated with penicillin. Of these 1116, 124 continued to have gonococci in urethral discharge after treatment.

Before treatment was given Curtis and Wilkinson measured the sensitivity to penicillin of 302 strains of gonococci by means of tube-sensitivity tests, which proved more accurate than plate tests. Of these strains 19·5% were sensitive to penicillin at levels of 0·125–0·5 units per ml. The failures of treatment after the injection of 300,000 units of procaine penicillin in watery suspension, or of procaine penicillin in oily suspension with 2% aluminium monostearate (P.A.M.), occurred, for the most part, with these relatively insensitive gonococci; in no case did failure occur when the sensitivity was below 0·03 units per ml. These significant findings have been confirmed by Cradock-Watson et al.,[6] who tested 200 strains of gonococci and found that 38 of them needed 0·128 units or more of penicillin per ml. for inhibition, and that patients infected with these strains were five times more prone to relapse after treatment than those infected with more sensitive strains.

In the discussion which followed the paper by Curtis and Wilkinson [7] it appeared that an increasing number of cases of gonorrhœa resistant to penicillin had been noted throughout London; but there was some doubt about the situation in the Provinces, for there had been no evidence of resistant cases at Newcastle or at Portsmouth. At Liverpool it has been customary in the past four years to treat male patients suffering from gonorrhœa with single injections of 0·5 g. of streptomycin. The numbers so treated were 215 in 1954, 231 in 1955, and 241 in 1956, and the results have been good. Nevertheless the proportion of failures increased from 2·3% in 1954 to 4·9% in 1955 and 7·0% in 1956. Alergant,[8] who reported these facts, had not attempted to demonstrate streptomycin resistance in vitro, but had little doubt that streptomycin-resistant strains of this organism were emerging. Curtis and Wilkinson,[5] in London, found only 1 streptomycin-resistant strain of gonococci among 81 tested; and Cradock-Watson et al.,[6] also in London, found none resistant among 200 tested.

The evidence suggests, therefore, that development of resistance is related to the local practice, with penicillin-resistance in London where penicillin has been the drug of choice and streptomycin-resistance in Liverpool where streptomycin has been the routine remedy. Further data are required, especially on tests in vitro in Liverpool; but these findings may point the way to a means of dealing with this difficult problem. The evidence is scanty; but, such as it is, it suggests that sensitivity may perhaps be restored if the drug is withheld from patients with the infection. Dunlop [9] showed that 86% of cases of acute gonorrhœa seen at the London Lock Hospital in 1946–47 were resistant to treatment with sulphonamides; but Cradock-Watson et al.,[6] who tested their 200 strains of gonococcus for sensitivity to sulphathiazole, found to their surprise that 199 of them were inhibited by 8 mg. or less of sulphathiazole per 100 ml.

A concerted policy of changing from one remedy to another in selected areas, at agreed intervals, might help to preserve the efficacy of these drugs; but much more information is required before such a plan can be advocated with confidence. Cradock-Watson et al.[6] are meeting the immediate problem by increasing routine dosage of procaine penicillin for the treatment of gonorrhœa from 300,000 to 600,000 units. Curtis and Wilkinson [5] also recommend increasing the dosage of procaine

1. Wilkinson, A. E. *Brit. J. vener. Dis.* 1958, **34**, 81.
2. Campbell, D. J. *Brit. med. J.* 1944, ii, 44.
3. Ministry of Health. Report on the State of the Public Health, 1956, Part II; pp. 63, 252. H.M. Stationery Office, 1957.
4. King, A. *Lancet*, 1958, i, 651.
5. Curtis, F. R., Wilkinson, A. E. *Brit. J. vener. Dis.* 1958, **34**, 70.
6. Cradock-Watson, J. E., Shooter, R. A., Nicol, C. S. *Brit. med. J.* 1958, i, 1091.
7. *Brit. J. vener. Dis.* 1958, **34**, 78.
8. Alergant, C. D. *ibid.* p. 36.
9. Dunlop, E. M. C. *ibid.* 1949, **25**, 81.

penicillin in watery suspension from 300,000 units to 600,000 or 1,200,000; but they believe that efforts should be made to devise a preparation of penicillin which would give a blood-level of not less than 1 unit per ml. for not less than twenty-four hours—though preferably for not much longer, owing to the risk that long-lasting low levels of penicillin may produce more resistant strains of gonococci or symptom-free carriers. These methods are unlikely to provide more than a temporary solution. Although the gonococcus is susceptible to many other antibiotics, their cost is likely to be prohibitive since gonorrhœa is so prevalent.

Morton [10] has suggested that further research should be undertaken into the possibility of active immunisation against gonorrhœa. If it proved possible to produce an effective vaccine, that in itself would raise fresh difficulties —not the least of which are the ethical issues that are apt to be involved in any prophylaxis of venereal disease applied before exposure to the risk. But, at least in so far as the proposal, if implemented, would necessitate a detailed study of the organism, it is to be welcomed.

REHABILITATION

DURING the year 1957, 9627 people (8310 men and 1317 women) entered the fifteen industrial rehabilitation units (I.R.U.S) provided by the Ministry of Labour and National Service.[11] A recent account [12] emphasises once again the value of this form of social rehabilitation.[13 14]

An increasing number of entrants—now 70%—are recommended by medical sources (hospitals, general practitioners, and regional medical officers, in that order). Of those recently sick or injured, and referred by employment exchanges, it is stated: "It would no doubt have been preferable for many of these cases to have been recommended by the doctor in charge of their medical treatment or by a resettlement clinic . . ."

The material was by no means promising. Of the total entrants, 68% were of the semiskilled or labouring classes, while only 18% were skilled. Some 30% had not been in regular employment for the previous two years; and, of these, 14% had not been in regular employment for at least five years. The fact that, of 19% who failed to complete their courses, more than half failed for medical reasons suggests that better selection of disabled persons and an appreciation of the real function of these I.R.U.S by the medical profession would be economically sound and therapeutically rewarding. That cases of respiratory tuberculosis show the lowest premature-termination rate and the greatest success in resettlement is tribute perhaps not so much to the patients themselves as to chest physicians, whose continuing interest in industrial rehabilitation is well known and made manifest by their enthusiastic use of resettlement clincs. Psychosis and psychoneurosis, not unexpectedly, are associated with a high rate of premature discharge. Other groups, apart from respiratory tuberculosis, which afforded few problems in placement were diseases and injuries of upper and lower limbs; those with a low rate of success included arthritis, diseases of the cardiovascular system, and diseases of the central nervous system such as disseminated sclerosis and cerebral palsy.

Of those completing a course, some 82% had been placed or had started training within six months. Satisfaction, and even surprise, might be felt at a success-rate of the order of 80% in neurosis, psychosis, and epilepsy; but selection may be operating outside as well as within the I.R.U.S. Those recovering from recent sickness or injury, whether referred by doctors or by disablement resettlement officers, did better both in completing courses and in obtaining employment than those who had been unemployed for some time. The importance of early rehabilitation has previously been noted by Ferguson and McPhail [15] and by Mair and Reid.[16] Not every disabled person requires such help, but many do. Early resettlement, the use of I.R.U.S, and active guidance towards social independence, with the aid of almoners, is as much a medical responsibility as is early ambulation in the prevention of pulmonary embolism. Neglect of the former may have consequences hardly less serious than neglect of the latter.

OUTPATIENT WAITING-TIMES

FOLLOWING stimuli in 1949 and 1954, the Minister of Health has prodded hospitals again about their outpatient waiting-times. This time, however, the prod is rather different, since it is based on a report [17] of the Ministry's own Organisation and Methods Service. The report, the first of a series, deals with appointment systems in outpatient departments, and at the outset declares "In most cases our first aim has been to obtain facts about the extent of any waiting under the existing conditions. . . ." Unfortunately the facts collected are withheld, and the extent of waiting-time is not disclosed. Instead the report reiterates some familiar advice, much of which was mentioned in 1949 and 1954, and all of which must be well known to the staffs of hospitals trying daily to deal with this intractable problem.

In 1952 we published an article [18] from the Nuffield Provincial Hospitals Trust which showed that patients were having to wait about an hour in outpatient departments for their consultations. Since then such evidence as has been published gives the impression that some improvement has taken place. It would, therefore, have been invaluable to know the present position; particularly as the O. & M. survey covered no less than five hospitals and a number of clinics as well. Has any improvement taken place? If so, how great is it? The occasion calls for an assessment of any improvements there may have been. If these improvements are inadequate (and the withholding of the facts is bound to create some suspicion that all is not well) then it is surely best, in a matter of such vital concern to the prestige and efficiency of the National Health Service, to say so. The repetition of what has been said before needs justification as well as the force of new evidence.

10. Morton, R. S. *ibid.* 1958, **34**, 81.
11. Annual report of the Ministry of Labour and National Service for 1957. Cmnd. 468. H.M. Stationery Office, 1958. 8*s*.
12. *Minist. Lab. Gaz.* August, 1958.
13. *ibid.* August, 1953.
14. Report of Committee of Enquiry on the Rehabilitation, Training, and Resettlement of Disabled Persons. Cmd. 9883. H.M. Stationery Office, 1956.
15. Ferguson, T., McPhail, A. N. Hospital and Community. London, 1954.
16. Mair, A., Reid, J. J. A. *Scot. med. J.* 1957, **2**, 467.
17. Outpatient Waiting Time. Ministry of Health Organisation and Methods Service report no. 1. H.M. Stationery Office, 1958. 1*s*. 3*d*.
18. Welch, J. D., Bailey, N. T. J. *Lancet*, 1952, i, 1105.

THE INDEX and title-page to Vol. I, 1958, which was completed with THE LANCET of June 28, is published with our present issue. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Special Articles

EARLY DIAGNOSIS OF CANCER

A Psychological Problem *

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MY interest in cancer education was first aroused in the early '30s, when a patient was sent to me as a possible carcinoma of the cervix.

She had a history of slight bleeding two years previously and again two weeks before the visit. Nothing abnormal was found on clinical examination, but I advised an examination under an anæsthetic. Unfortunately the patient was due to go on holiday with her husband to the South of France next day; so I said that if there was the slightest return of symptoms she must come home at once and that in any case she must see me when she returned. It was seven months before she again visited me, and then she said that she had been bleeding almost continuously. She added, "Do you know why I didn't come? Because I thought it was cancer". She had by then a third-degree endocervical carcinoma of the cervix and she lived two years. She was the wife of a surgeon, a very intelligent woman, a graduate, a member of a very intelligent family. In theory I had done the correct thing, but I have never forgiven myself for allowing her to slip through my fingers.

This incident made me realise that intelligence, and indeed sometimes even knowledge, has nothing to do with a patient's willingness to seek early diagnosis. It is a psychological problem; for cancer, unlike any other disease, is surrounded by a psychological atmosphere. I call it "cancer smog".

PHOBIA AND APPREHENSION

In true cancerphobia the person is so obsessed by fear of the disease that the obsession interferes with his way of life. I believe that there are very few of these, though each year one or two commit suicide. This term is used much too freely, and some doctors will label a patient a cancerphobe if the word "cancer" is mentioned.

But, though true cancerphobia is rare, I believe that nearly everybody suffers in some degree from cancer apprehension, which may take one of two forms.

Personal apprehension.—A person notices a slight symptom for which there is no obvious explanation, and thinks: "Is this cancer?" Often he or she dare not go to a doctor, and continues to worry until the pain ceases. Others who go to a doctor do not give the true reason for their visit: when they are not reassured, they return week after week and are diagnosed as neurasthenics when the real diagnosis is cancer apprehension. Sometimes, if the patient is brave enough to mention the word "cancer", the doctor, with the best of intentions tries to laugh away his fears. The result is that the patient feels a fool, never mentions the word again but goes on worrying. More than once after a lecture one of my audience has said: "I could not go to my doctor about cancer. I hate being laughed at."

I saw many apprehensive people in my outpatient sessions, and it was my rule after examining them to say: "I am glad to tell you there is nothing serious, and no evidence of *cancer*"—taking care to emphasise the word "cancer". Often the patient replied: "Thank God; that was what was really worrying me." It is impossible to say how many cases there are of this type of apprehension because they do not talk about it. Much of this personal kind of apprehension can be prevented by education.

Impersonal cancer apprehension.—By this I mean "fear of creating fear", by speaking about the disease or even mentioning the name. This is very common indeed, and it can be demonstrated by asking a lecture audience how many of them, if they had cancer, would like to be told the truth. Nearly all of them will hold up their hand. To the next question, "How many of you think that a friend or relation should be told?", scarcely anybody raises a hand.

Again, when our small Cancer Information Association was started in Oxford members were asked to send pamphlets to their friends, and stamped envelopes were enclosed for the purpose. Many refused because they said that their handwriting might be recognised, yet these same people readily supplied the names and addresses of their friends, provided that their own names were not mentioned.

This type of apprehension does much harm, by keeping up the conspiracy of silence and hush-hush, and thus preventing people from seeking advice.

ATTITUDE OF THE PUBLIC

Despite their apprehension, the public appear to welcome information on the subject if it is presented to them in the form of lectures, pamphlets, and newspaper articles. It is difficult to back this impression by full-dress statistics, but small inquiries seem to confirm it. In Manchester, for instance, of 1200 women who were asked (about cancer): "Do you think that there should be freer public discussion of its symptoms and possible cure?" 76% replied Yes, 9% No, and 15% were doubtful.[1] At the end of each lecture in a series given in Yorkshire, the following voting paper was distributed:

"Some people have suggested that lectures such as you have just heard do no good, and indeed may do harm. Please state quite frankly what effect it has had on you by putting a X against statement (i) if you think it has increased your worry and that such lectures should not be given; or against (ii) if it has helped you and you think that more such lectures should be given."

The result of 5740 votes was 99·1% in favour, 0·2% against, 0·7% doubtful.

REACTION OF THE DOCTORS

In 1953 the British Empire Cancer Campaign sent a questionnaire to every general practitioner (some 19,000) in England and Wales. They were asked to answer Yes or No to the question whether they approved of cancer education among the public. 14·1% said No, and 11·3% Yes; but, as 74·6% abstained, these figures are of little value.

In the same year the Ministry of Health sent a letter to 146 local health authorities urging them to start cancer education schemes, but so far only about 17 seem to have made any effort whatever. The most common excuse for this inaction is that the medical profession in the area are against it.

It is of course quite right that doctors should ask for statistical evidence that cancer education is of value, but it is a little difficult to see how the data can be obtained if the medical profession discourages any such education being carried out. Moreover, though some doctors are genuinely doubtful of its value, others oppose it on less objective grounds. Some think that most lay people are

* Part of an address given to the Section of Obstetrics and Gynæcology of the Royal Society of Medicine on Feb. 28, 1958.

1. Paterson, R., Aitken-Swan, J. *Lancet*, 1954, ii, 857.

fools incapable of understanding medical matters; others do not like being asked questions, and resent a request for a second opinion. Others fear that their crowded surgeries will become more crowded. But our experience in Manchester and in Yorkshire has proved this fear to be unfounded.

METHODS OF CANCER EDUCATION

The best way of spreading information is by word of mouth. This can be done by lectures, by discussion groups, or by the nursing profession.

During 1957 I gave 74 lectures, chiefly to Women's Institutes, the Red Cross, Rotary clubs, and other voluntary organisations within sixty miles of Oxford. 69 have already been booked for 1958. Such lectures should be illustrated (e.g., by flannelgrams) and plenty of time should be left at the end for questions. Pamphlets should be distributed or sold. Unfortunately few doctors are prepared to give lectures of this kind.

Conversation between the public and district nurses, health visitors, and midwives, is an effective means of carrying out cancer education, because these nurses are the friends of the people and are welcomed into their homes. A successful experiment of this kind has lately been made in York.[2] Such instruction costs very little, but the M.O.H. must be sufficiently interested to organise schemes of this kind.

The written word is also essential. Pamphlets must be written in the simplest of language. It is encouraging that some of the large national newspapers have published articles on cancer. Other methods such as posters, page-turning machines, and films are valuable but cost money.

Apart from saving lives, it must be of great benefit to the nation to diminish fear of this disease. Those of us who have spent many years on cancer education have proved the truth of Emerson's words, "Knowledge is the antidote to Fear."

PUBLIC OPINION ON CANCER

Changes following Five Years of Cancer Education

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AN experimental scheme of public education has been in operation in a defined test area under the Manchester Committee on Cancer for over five years. An attempt is being made to measure its impact in as many ways as possible. One index would be a demonstrable change of public opinion in line with the educational pattern pursued. We describe the results of an evaluation of this factor through a public opinion poll in 1957 carried out on similar lines to the one in 1953 (Paterson and Aitken-Swan 1954). The results of the present study are contrasted with three similar opinion polls: a simultaneous identical survey in a control area, the previous Manchester survey, and a Canadian survey.

Experimental and Control Area Surveys (1957)

The organisation of the education campaign in the experimental area has been described by Paterson et al. (1954). The precisely defined area was centred on Oldham, Rochdale, Bury, and Ashton-under-Lyne. The contrast study was made in a previously defined control area, similar in size and in social and industrial structure, centred on Preston, Blackburn, and Wigan, in which there was no planned cancer education. The contrast between these two areas is, therefore, the most valuable direct evidence of the effectiveness of the efforts made in the experimental area. The organisation which had carried out the Manchester survey in 1953 undertook the present surveys, using largely identical questions. The order in which questions were asked was intended to conceal that the inquiry concerned cancer until answers had been given to some preliminary questions.

A randomly selected sample of just under 1200 women, aged 21 and over, were interviewed in each area, their addresses being spread over the three main towns and the rural district. As in the Manchester survey, the women interviewed were interested in the inquiry and gave their full cooperation.

Manchester Survey (1953)

This was carried out amongst a representative sample of 1200 women, aged 21 and over, living in Manchester, Salford, and Stockport (Paterson and Aitken-Swan 1954). There had been no recent campaign of cancer education. Unlike the experimental and control area surveys, the Manchester sample covered a city population only. But this study can be reasonably taken as exemplifying the state of opinion five years ago, before any educational scheme was launched.

Canadian Survey (1954)

Using the same questionnaire as in our Manchester study, the Canadian Institute of Public Opinion made this survey on behalf of the Canadian Cancer Society (Phillips 1955). The results quoted later are from a national sample of 2000 cases, interviews being distributed proportionately between the provinces. Canada has been exposed for many years to extensive cancer education. These figures give some indication, therefore, of the state of opinion in this field after years of educational work, and serve as a useful target for ourselves.

Results

The results of the inquiry are set out in three main sections:

(*a*) Opinion on curability and on the value of treatment.
(*b*) Knowledge of symptoms.
(*c*) Impact of the campaign.

All the figures are in percentages and may add up to over 100 where more than one reply was given.

OPINION ON CURABILITY OF CANCER AND VALUE OF TREATMENT

(1) *What to you is the most alarming of the following diseases: heart trouble, tuberculosis, asthma, cancer, rheumatism?*

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Cancer	74	78	70	67
Tuberculosis ..	10	8	19	7
Heart trouble ..	9	8	12	24
Asthma ..	4	4	3	2
Rheumatism ..	4	2	3	2

Cancer was rated the most alarming disease in all the surveys. Fewer women now than in 1953 put tuberculosis first, and the raised figures for cancer in 1957 are probably only a reflection of the lowered tuberculosis figures.

(2) *Can cancer be cured or not?*

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Yes {usually / sometimes} ..	55	46	36	63
No, never	30	41	50	30
Do not know ..	15	13	14	7

2. Crane, C. B. *Nursing Mirror*, June 28, 1957, p. 2.

In comparison with the Manchester (1953) survey, the experimental area shows an increase of 19% in the proportion aware that cancer is sometimes cured against, in the control area, an increase of only half as much (10%). This difference can be regarded as a consequence of the educational campaign because the results for tuberculosis and heart trouble are practically identical for the experimental and control areas, both as to actual figures and as to increase since 1953. The percentages of people replying that tuberculosis and heart trouble are "usually" or "sometimes" cured were as follows:

	Experimental	*Control*	*Manchester (1953)*
Tuberculosis	88	89	80
Heart trouble	56	56	49

(3) *Do you think early treatment of cancer increases the chance of a cure or does it not make any difference?*

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Increases the chance	71	66	57	80
Makes no difference	18	24	29	15
Do not know ..	11	10	14	5

The results, though overall not as definite as those of question 2, conceal an interesting contrast in the answers given by social class and age categories. In the experimental area, the higher social classes and those aged 50 or more show a considerable increase over the control area in the proportion who think early treatment of value.

These three were the key questions of this section of the study. Others were less informative. As described by Paterson et al. (1954), the education was predominantly an attempt to put across the idea that nowadays *some* cancers are curable, and little emphasis was put on the symptoms. We feel that the answers to questions 2 and 3 are evidence that this has produced, though in modest degree only, a real change in public opinion. The key figures—experimental and control percentages accepting cancer as "sometimes curable" at 55 and 46% respectively—are statistically highly significant ($P = <0{\cdot}001$).

KNOWLEDGE OF SYMPTOMS

There was little or no difference in the answers to questions on symptoms between the experimental and control areas, and little change since 1953. Questions were asked in several ways to try to get a true picture, though not all are shown here.

(4) *Which of these symptoms would strike you as the most alarming?*

(*a*) Constant cough.
(*b*) Lump in the breast which does not hurt.
(*c*) Losing weight.
(*d*) Seeing a show of blood or discharge ten years or so after the change of life.
(*e*) Frequent pain after eating.

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Painless lump ..	37	39	39	38
Losing weight ..	20	19	24	10
Constant cough ..	16	16	17	16
Show of blood ..	19	19	16	27
Pain after eating ..	6	7	7	7

In all the surveys this question was asked before it was known that the subject of the inquiry was cancer. A painless lump in the breast was regarded as the most alarming symptom by women of all ages. The results do not suggest that for the past five years an intensive campaign has been going on in the experimental area which might have enlightened women about the possible significance of a painless lump in the breast, or unusual bleeding, or discharge. This may be because of the priority given to building up belief in cure, and an attempt not to pin education to "danger sign symptoms".

(5) *If a friend told you she had a lump in the breast what would you think it meant?*

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Cancer mentioned ..	51	51	59	62
Growth or tumour ..	14	17	20	20
Immediate attention necessary, something seriously wrong	14	12	3	8
Cyst or abscess ..	16	12	16	8
Other	6	4	6	7
Do not know ..	17	18	14	14

(6) *If a friend told you she had seen a show of blood or discharge ten years or so after the change of life what would you think it meant?*

Answer	Present study		Previous studies	
	Experimental (%)	Control (%)	Manchester (1953) (%)	Canada (%)
Cancer mentioned ..	23	21	19	45
Growth or tumour ..	8	7	5	7
Something seriously wrong, needing urgent attention	11	12	7	11
Nothing to worry about..	5	4	8	1
Fibroid, cyst, &c. ..	15	14	19	7
Do not know	44	46	46	33

Many women gave more than one answer, hence the summated percentages above 100. Analysis by age shows that the proportion taking the symptom of hæmorrhage seriously was significantly higher amongst those aged 50 or more in the experimental area than in the same age-group in the control area.

The final questions about symptoms were put to the total sample of the experimental and control areas. In the Manchester (1953) survey they were asked only of the group who, in reply to an earlier question, had said that the breast or womb was the most common site of cancer in women. The latter results cannot, therefore, be used for comparison.

(7) *Can you tell me what the first signs of cancer of the womb are?*

	Experimental	*Control*
Bleeding	18	24
Discharge	13	14
Pain	6	7
Other	3	3
Do not know	65	61

(8) *Can you tell me what the first signs of cancer of the breast are?*

	Experimental	*Control*
Lump(s), painless lump, painful lump, swelling	67	73
Pain	5	4
Other	5	5
Do not know	29	25

At first glance these are curious and unexpected results. They could be interpreted as implying that in an area where there has been five years of cancer education there is rather less knowledge about the symptoms than in the control area. They could, however, equally be interpreted as a consequence of teaching which, wherever it stressed significant symptoms, consistently linked this with the emphasis that "these do not necessarily mean cancer by any means—they merely mean that

you should see your doctor and be examined". This would also explain the absence of difference between experimental and control areas shown in the answers to questions 4, 5, and 6.

IMPACT OF EDUCATIONAL CAMPAIGN

In addition to its primary purpose of testing public opinion, the poll enabled us to estimate the coverage achieved by the campaign, and some further questions were asked in the new surveys. After finding out whether the women interviewed knew if doctors had given any talks on health problems to any of the women's societies in their town in the past few years, they were asked:

(9) *Have they ever talked particularly about cancer at any of these meetings?*

	Experimental	*Control*
Heard of talks on cancer	8	1

After five years of education, therefore, only 8% of a representative sample, and hence presumably of the population in the experimental area, had heard of talks on cancer being given. 4% had attended a talk. But practically all the talks were given at the routine meetings of organised societies of different kinds, and not at public meetings. A more correct denominator is, therefore, the membership of these organised groups, as shown in question 10:

(10) *Do you belong to any women's group attached to church or chapel, or to any other women's group that holds regular meetings?*

	Experimental	*Control*
Yes	11	15

In the experimental area 8 out of every 11 members of societies had been reached, as compared with 1 in 15 in the control area. But the 11% shows that concentration on this group touches only the fringe of the problem, and that there is a great need to extend the coverage by other methods—e.g., factory lectures.

(11) *Have you read or seen anything about cancer or reports of meetings about cancer in any local paper?*

	Experimental	*Control*
Yes	39	19

If the figure of 19% in the control area be regarded as representing the "normal" background, the figure of 39% for the experimental area shows that an additional 20% coverage of the population has been achieved by the campaign's own publicity in local newspapers.

Answers to a further question showed the proportion of women who recalled reading about cancer in the national morning and Sunday newspapers, women's weeklies, and other magazines:

(12) *Have you read or seen anything about cancer in the national papers or any of the women's "books"?*

	Experimental	*Control*
Yes	43	40

Both areas are far from being free of general cancer literature, therefore, and despite the absence of any planned national cancer education there is a constant background of individual miscellaneous information in circulation. Since this already reaches 40%, much more might be achieved by planned publicity on a national scale.

Discussion

Since the Manchester survey of 1953 considerable publicity has been given to cancer in national newspapers and magazines, as shown by question 12. People might be expected to be better informed in 1957 than in 1953 apart from any special efforts. If the intensive campaign has been effective, women in the experimental area should be still better informed. Some of the results show that this is so. Compared with the Manchester (1953) survey, both the 1957 surveys show a greater acceptance of cancer as not always incurable, and of the fact that early treatment increases the chance of cure. This is significantly greater amongst women in the experimental area than in the control area, the actual figure approaching that found in Canada, which has been continuously exposed to education of this kind for many years.

Surprisingly, the results for questions about the symptoms of breast and cervical cancer remain similar or favour the control area. We have suggested that the emphasis that these signs call for medical advice but are "of course" quite often due to other things, has successfully avoided the "danger sign" fear-provoking approach. The proportion of women aware that a lump in the breast can be a sign of cancer was high in 1953 and is no higher in 1957. Ignorance of the early symptoms of cervical cancer, common in 1953, is unaltered in the population as a whole, although the answers to question 6 show some improvement in the age-groups over 50 in the experimental area.

Answers to the questions on the most alarming disease suggest that the campaign has not added to the fear of cancer. Indeed, fewer women in the experimental than in the control area thought cancer the most alarming of the five diseases (question 1), and over three-quarters thought that there should be freer public discussion of it.

These results, obtained by the opinion-survey method, are valid as far as an adequate and representative sample and trained interviewers can make them. But it still has to be shown whether women in the experimental area, who presumably have an improved outlook on the curability of some cancers and on the value of early treatment, act upon their knowledge and seek medical advice more promptly than do those in the control area. The results of further inquiries along these lines into the effects of the campaign will be analysed in a later article.

Summary

In 1957 a survey of public opinion was made in an "experimental area" and in a comparable control area after five years of intensive cancer education. The results of these surveys are contrasted with those of two similar surveys, one made in Manchester in 1953 and the other in Canada in 1954.

In the experimental area there has been a statistically significant improvement in the proportion of women aware that cancer is not always incurable, and who think that early treatment increases the chance of cure. Questions asked about symptoms do not reveal differences between the experimental and control areas, except that in the age-groups over 50 significantly more women in the experimental area took the symptom of hæmorrhage seriously.

Questions to test awareness of the campaign for cancer education showed that 8 out of every 11 members of women's organisations had heard of talks on cancer and 4% had attended a talk. 39% had seen educational articles in local newspapers.

Copies of the complete analysis of the English surveys may be had on application to the Director, Christie Hospital and Holt Radium Institute, Manchester, on receipt of 5*s*. (free to applicants from a foreign country where currency transfer is difficult).

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THE DEFENCE SOCIETIES

AT their annual general meetings this year the two English medical defence societies both reported an increase in expenditure, largely due to the heavier damages which are being awarded as the result of the depreciation in the value of money.

MEDICAL DEFENCE UNION

Speaking at the meeting of this society, which was held in Newcastle upon Tyne on Sept. 16, Mr. A. HEDLEY WHYTE said that, though young doctors found it difficult to imagine that they would ever be unlucky enough to make a wrong diagnosis, misinterpret an X-ray film, or perform an incorrect operation, their seniors were aware that every day something was going wrong with some poor doctor somewhere. It was a relief to know that all the time the M.D.U. was busy trying to straighten out these difficulties and to see fair play and justice done to both sides, if possible. No branch of the profession was inviolate; but as "doers" surgeons were perhaps peculiarly vulnerable, and Mr. Hedley Whyte described the procedures which had been devised at the Royal Victoria Infirmary to safeguard the identification of patients, the counting of swabs, blood-transfusions, the administration of anti-tetanus serum, intramuscular injections, and the numbering of fingers and toes. The important thing was to ensure that the right treatment was given to the right patient at the right time.

At the end of 1957 the Union had 44,543 members and the total funds available were £150,000. During the year expenditure exceeded income by £19,000, despite an increase in subscription income of over £4000. As a result the council have been obliged to raise the subscription from £2 to £3 with effect from May 1, 1958.

The president is Dr. S. Cochrane Shanks and the hon. treasurer Dr. Henry Robinson. The secretary is Dr. Robert Forbes, and the address of the Union is Tavistock House South, London, W.C.1.

MEDICAL PROTECTION SOCIETY

Presiding at the annual general meeting, held in London on Oct. 1, Sir ERNEST ROCK CARLING said that 1957 had been a year of progress during which the society's work overseas had been greatly extended. The depreciation of the value of money had given rise to a tendency for the Courts to award larger sums for compensation and damages; but he was glad to say that it was not, at any rate for the present, necessary to raise the subscription. Turning to the "embarrassments, misfortunes, and lapses of memory" that led some members into trouble, Sir Ernest stressed the importance for their defence of full, accurate, and contemporary records. It was, he said, particularly important that doctors should keep separate records of their private and National Health Service practice.

Mr. W. G. HAWKINS, of Messrs. le Brasseur and Oakley, the society's solicitors, said that after ten years' experience it was clear that the N.H.S. had increased the work of the society. Not only was more litigation initiated by patients but new tribunals and committees of inquiry had been set up at which doctors often needed legal representation. Doctors and dentists also sought the society's advice on questions of remuneration and superannuation. Mr. Hawkins had noticed that in the many cases which turned on an alleged failure in diagnosis the commonest conditions were fractures and dislocations and tuberculosis. The use of X-ray apparatus in diagnosis was common to both, and it was usually alleged that the doctor had not taken an X-ray or had not taken one soon enough. Later in the meeting Prof. LAMBERT ROGERS, speaking as a teacher of surgery, reminded members that in the past few years we had learnt more of the dangers of accumulated radiation. A balanced judgment must be used in ordering X-rays, and they should never be used merely as a cover against a possible legal claim. Sir ERNEST ROCK CARLING added that a Government committee was studying the problem, and that progress had already been made in devising adjustments which would allow radiographers to use smaller fields and smaller dosages and yet obtain better results.

The income of the society for the year amounted to £82,500—an increase of £16,500 over last year. The total income from all sources was £94,000 and exceeded expenditure by £7000, though expenditure, at £87,000, had risen by £18,000 compared with 1956. Legal expenses of defending and conducting cases for members had increased by £4600, and the indemnity account by £8500. The membership had risen from 30,291 in December, 1956, to 33,437 in December, 1957.

The society's officers were re-elected—Sir Ernest Rock Carling as president, Mr. W. M. Mollison as treasurer, and Dr. A. R. French as secretary. The chairman of council is Dr. F. Harwood Stevenson, and the deputy secretary Dr. H. A. Constable. The offices, from which the latest annual report may be obtained, are at Victory House, Leicester Square, London, W.C.2.

Conferences

CHILD NEUROLOGY

THE first International Study Group on Child Neurology and Cerebral Palsy was held in Oxford on Sept. 21–27 under the auspices of the National Spastics Society.

Dr. C. KOUPERNIK (France) said that in the past twenty-five years considerable advances had been made in the investigation and treatment of neurological disorders in the young. In the past the techniques used had been those of adult neurology and no account was taken of the dynamic processes of development in infancy. Furthermore, cerebral palsy and other brain disorders were for the most part explained in terms of congenital syphilis or degeneration. This led to an attitude towards the crippled child compounded of rejection and therapeutic abstention. It was significant that the word rehabilitation did not appear in the textbooks of the early thirties. Today our approach to cerebral palsy was rightly much more a functional one, and the biochemist would undoubtedly play an increasingly important role. Treatment was not simply a technical matter. Thus in some we had to deal with specific learning difficulties and distorted perception. Psychotherapy had its part to play. Admission to hospital and other institutions should be avoided, especially in the young; the mother was probably the best therapist. Dr. Koupernik summed up by saying there was a time when child neurology was an arid and hopeless subject. Now it was oriented towards research and rehabilitation; it was becoming more and more dynamic.

Hypertonus

Dr. R. C. MAC KEITH reminded his audience that spastic hypertonus might present in one of several ways: as a resistance to movement in one direction which on steady pressure gave way either slowly or suddenly; or as a sudden resistance (or catch) on more or less brisk movement. Hyperreflexia was significant when one-sided or when associated with other supportive evidence. Spasticity in the child, unlike that in adults, could change from one moment to another. It might be influenced by such factors as fear, coldness, and body posture.

Dr. T. T. S. INGRAM said that muscle tone and posture were interdependent; but the effect of one on the other became less as the infant matured. He was able to define in the normal baby four overlapping developmental stages, based broadly on changing patterns of posture and tone.

Dr. J. H. CROSLAND pointed out that treatment, although never curative, can ameliorate spasticity, thus leading to an increase in power in the affected muscles and, at the same time, to lessening of the functional disturbance. Stretching of hypertonic muscles was still the method of choice, and in the case of the legs walking calipers of the right kind could help to achieve this effect. At the same time exercises should be directed to the stretched and weakened antagonists.

Dr. J. A. V. BATES described the results of cerebral surgery in the adult for selected motor disorders. The surgeon's aim was to make a destructive lesion in the presumed disordered

area. Longstanding tremor and rigidity could be relieved immediately without disturbing fine voluntary movement. Complications such as hemiplegia were most unusual. The technique had been tried in various spastic and athetoid conditions in childhood, so far with disappointing results. This empirical approach posed more questions than it had answered.

Dr. C. G. PHILLIPS, Dr. P. B. C. MATTHEWS, and Dr. G. RUSHWORTH described the effects of activity of gamma motor neurones on hypertonus. Motor neurones were of two types: (1) alpha, supplying main muscle fibres; and (2) gamma, the specialised muscle-fibres within muscle-spindles. Activity of gamma fibres did not directly produce tension in muscle but increased the afferent proprioceptive discharge of muscle spindles, which could in turn affect muscle tone by reflex excitation of alpha motor neurones. It now seemed likely that hypertonus might in some cases be due, at the spinal level, to hyperactivity of gamma motor neurones increasing to an abnormal degree the sensitivity of the proprioceptive endings of the stretch receptors of muscle spindles.

Development of Central Nervous System

Prof. J. BOYD gave a fascinating account from the point of view of an experimental embryologist of the development of the forebrain and cerebral cortex in vertebrates, including the human embryo. He described the influences emanating from adjacent structures on the growth of the spinal cord and contrasted them with differing ones acting on the forebrain. He suggested how interference with one of these inductive mechanisms might lead to a specific brain anomaly.

Dr. J. N. CUMINGS reviewed lipid chemistry of the young and growing brain, particularly in relation to the onset and progress of myelination. His studies suggested that myelination was particularly active from three months to seven years, which was at variance with the histological estimate. He was not aware of any data regarding lipid abnormalities to be found in cerebral palsy.

Dr. D. RICHTER considered the role of enzymes in the development of the central nervous system. He said that during early fœtal life brain growth was rapid and enzymes systems concerned with protein and lipid synthesis were active. Later, other systems developed which were apparently concerned with the " metabolism of function ". However, studies with labelled aminoacids suggested that protein synthesis continued after neural growth had ceased. The first function of the brain was as a neuro-endocrine regulator dealing with slow humoral processes. Later speed of reaction became important, and it functioned more as a computer. Changes of this kind probably depended ultimately on enzyme maturation. The total number of enzymes in the brain might be of the order of 10,000. It was therefore not surprising that sometimes an enzyme was found to be deficient or missing. This could be recognised in phenylketonuria where there was a large metabolic effect; but there might be other errors where a deficiency or imbalance in an enzyme system might be less readily detected.

Clinical Approach to Classification

Prof. A. GRISONI-COLLI (Italy) said that more important than a change of classification was a detailed definition of physical signs using a standardised terminology. She based her rehabilitation programme on the interpretation of the various neurological features found in the individual case.

Prof. R. S. ILLINGWORTH said that he could see no reason to alter the classification suggested by the American Academy of Cerebral Palsy, which was widely accepted in the U.S.A. and elsewhere.

Electroencephalography in Cerebral Palsy

Dr. G. PAMPIGLIONE said that electroencephalography was of little value in the prognosis and treatment of cerebral palsy itself, although it might well uncover a latent epileptic tendency. A discussion ensued about the wisdom of using anticonvulsants in cerebral-palsy cases for an epileptic diathesis revealed by electroencephalography. The majority view was that, because of the risk of unpleasant side-effects, such drugs should be reserved for manifest epilepsy.

Examinations in the First Year of Life

Dr. P. E. POLANI described a method for the detailed neurological examination of the newborn according to the work of André Thomas. Much of the examination depended on assessing tone through static postures and passive mobilisation with optimum relaxation. A wide range of reflex responses could then be studied. Care must be taken not to do harm through injudicious handling, especially in frail premature infants. Little was known about what diagnostic and prognostic inferences could be drawn from isolated neurological signs. We were still at the stage of defining the broad range of normal behaviour. Physical signs must, of course, be interpreted against the background of a detailed history. Asymmetrical changes were likely to be significant. All-important was a careful follow-up of babies considered to be at risk.

Dr. A. MINKOWSKI (France) and his co-workers had found a correlation between the oxygen content of fœtal blood at birth and the incidence of abnormal neurological signs in the early neonatal period; the greater the degree of anoxia the more often was abnormality found. Dr. J. P. N. TIZARD wondered how accurately an isolated oxygen determination on a cord venous sample before the first breath portrayed the state of affairs in the infant's circulation.

There appeared to be a wide divergence of opinion between French and English clinicians about the best treatment of intracranial birth injury. Dr. MINKOWSKI felt convinced that repeated lumbar punctures until the cerebrospinal-fluid constituents approached normal were helpful in these cases. In this country conservative treatment was favoured.

Professor ILLINGWORTH described a follow-up study of children thought in infancy to be mentally retarded on the basis of Gesell testing. The diagnosis had been fully confirmed in over 90% of cases by intelligence-quotient tests at the age of 5 years or more. Although many psychologists thought otherwise, he believed developmental tests had a high predictive value. A series of infants whose precocious behaviour had been detected in the early weeks of life were followed through with the help of a film. These babies were all shown to be walking by the age of 10 months. Professor Illingworth was careful to point out that superior intelligence could not be predicted on this basis. Precocious speech, however, did seem to indicate superior ability. He stressed the wide range of normal development; thus a child might not walk until the age of 2 or 3 years and yet prove to be perfectly normal. On the other hand, a feeble-minded child sometimes showed normal motor development in infancy.

Specific Disorders of Mentation

Mr. R. V. SAUNDERS discussed the educational disabilities of children with cerebral palsy attending five different schools in his area. To avoid misplacements, a comprehensive case study of each child was necessary. This was best done by a team which should include a pædiatrician, a psychologist, and a social worker. Ideally the home should be visited so that the child could be seen in his natural setting.

Dr. MAC KEITH described a simple set of screening-tests to be used by pædiatricians for specific learning difficulties. He would forestall criticism by emphasising that these were not comprehensive and were not meant to replace the opinion of a neurologist or psychologist. If his suspicions were aroused on crude testing he would then ask for more skilled help.

Dr. W. RITCHIE RUSSELL thought the term body image was not a good one as it over-emphasised the visual aspect, and of course those born blind usually had an accurate idea of their body. The development of the body-image system in infancy probably depended largely on chance. Thus the infant at some

time put his fist in his mouth; and, as this gives rise to an agreeable sensation, the sensorimotor reaction was facilitated, repeated, and strengthened. Later, the eyes learnt to turn towards an object seen, and the hand learnt to move towards it, to grasp it, and to convey it to the mouth.

Dr. GRACE WOODS said that the development of body image was essential to normal development and behaviour. Various factors might influence the development of this function. Important among these were sensation, both epicritic and proprioceptive, and, above all, movement. Defects might be due to lack of movement, as in ill children who had been immobile from early childhood and those with cerebral palsy and poliomyelitis. It also could be due to damage in the parietal or possibly occipital lobes. It was perhaps significant that athetoids with their great mobility were less frequently affected than spastics. At the Bristol school they were coming to realise that spastic children needed as much freedom of movement as they could get.

POLIOMYELITIS

THE fifth European Symposium on Poliomyelitis was held in Madrid on Sept. 28–30, under the chairmanship of Prof. G. FANCONI.

Vaccination

In Germany epidemics of 3114 cases in 1955 and 4163 in 1956 stimulated parents to have children vaccinated in 1957. 631,650 were vaccinated, 85% of whom received two inoculations. Following vaccination 7 died; in none was poliomyelitis diagnosed, but 3 deaths (2 of patients with allergy and 1 of a child with whooping-cough in whom encephalitis developed) were attributed to vaccination.

Dr. A. PAYNE (W.H.O.) stated that most deaths within 4–6 weeks after vaccination were not attributable to vaccination, but in a small proportion anaphylaxis therefrom seemed a definite cause. All other delegates reported insignificant sequelæ of vaccination. In Denmark 98% of children have been vaccinated; the intradermal route for first doses is popular. In Czechoslavakia among approximately 2,500,000 vaccinated, the morbidity was a third of that in the unvaccinated. In 1957, Hungary vaccinated children at the beginning of the worst epidemic in her history. "The rate of incidence started to decrease at an earlier point of time than in the years before and than in the neighbouring countries"—and this although children received two doses of only 0·1 ml. of vaccine intradermally. In Great Britain vaccine with type-I Enders modification of Brunhilde, type-II M.E.F.1, and type-III Sanket was used increasingly, but demand necessitated import of other vaccines. The M.R.C. trial on 196 children with no detectable antibodies before vaccination showed in all but 2 satisfactory response. Satisfactory response to types II and III and a slightly less satisfactory response to type I was reported from Piedmont in a similar scientific experiment.

Dr. PAYNE reported that Israel had an epidemic of several hundred cases in 1958, affecting equally those unvaccinated and those vaccinated with Salk's vaccine and technique. Three doses, but certainly not two doses, "perhaps" had a slightly beneficial effect. In the Detroit epidemic the pattern was not yet clear, but there were a considerable number attacked among vaccinated children.

Dr. SVEN GARD (Sweden) discussed the immunity mechanism. Antibody response was directly proportional to antigenic strength. Some strains overlapped in their antigenic power. More delicate tests showed that apparent absence of antibody did not denote no previous exposure. Antibody levels high after vaccination could fall to zero; some strains, such as the Mahoney, were more invasive than others. The first inoculation must be powerful enough to sensitise the patient, and intradermal injections almost never achieved this object. Clinical immunity was proportional to antibody titre, which itself was proportional to antigenic stimuli; local resistance of mucous membrane due to natural infection produced an immune barrier and relative protection. The safest and most effective technique was subcutaneous injections of inactivated virus followed by oral live virus.

Dr. LOEFFLER (Switzerland) showed that immune bodies after vaccination can persist for a year but serology cannot by itself provide an index of clinical immunity.

Dr. J. TOBIN reported that the antigenic power of the British vaccine—i.e., with a substitute for the Mahoney strain—was as good as that of the American. Commercial vaccines were indifferent; and we wanted them three times, and in some instances six times, more potent than they were, especially as regards type I. The response in monkeys mimicked that in man.

Diseases Resembling Poliomyelitis

Dr. W. H. BRADLEY spotlighted ECHO type infections, which attacked 98 out of 2000 in the epidemic described by Pickles. In some epidemics the rash was characteristic—rubelliform but often patchy and confined to the face.

Prof. H. C. A. LASSEN (Denmark) said that in Denmark only 2 out of 90 had rashes. ECHO type-I virus was recovered from the fæces in 70 and cerebrospinal fluid in 20.

Dr. A. M. RAMSAY described Icelandic, Akureyri, or Royal Free disease. Electromyography distinguished it from poliomyelitis. The clinical course—especially the tremors and the sequelæ of proneness to fatigue and mental inertia and emotional instability, relapses of which were common with minor infections—was different, and he deprecated terming such patients hysterics.

Dr. GARD said that in Sweden recently they had had 67 patients with tick-borne encephalitis. The source was cattle along the East Coast.

Reablement

Dr. A. B. KINNIER WILSON emphasised that reablement of respiratory cripples depended on many factors, particularly the morale of the patient. The orthopædic surgeons were not united in recommending early or late treatment for deformities, but the general opinion was that early treatment should be applied where muscles were at fault and later treatment where bone growth was a feature.

Physiology of Motor Cells

Dr. W. RITCHIE RUSSELL said that 100,000 motor cells in the spine out of 10 thousand million in the central nervous system were our only cholinergic cells. The maximum rate of discharge of 100 per second was low. The old concept of an upper and lower motor neurone was outmoded by the discovery of intermediate cells. Every anterior horn cell sent many—perhaps a hundred—branches to muscle-fibres, and it was the power of these cells to send additional nerve fibrils to denervated muscle cells which probably explained their continuing power to recover strength for several months. The neurophysiologists agreed that passive movements in the early stages and active movements thereafter were useful.

BIOCHEMICAL RESPONSE TO PHYSICAL INJURY

AN international symposium on the Biochemical Response to Physical Injury was held at Semmering, Austria, on Sept. 7–12. This was organised by the Council for International Organisations of Medical Sciences (C.I.O.M.S.) with assistance from the Wellcome Trust and the International Union of Biochemistry and was under the chairmanship of Dr. D. P. CUTHBERTSON. There follows a brief report of some of the contributions.

Biochemical Changes in Injured Tissue

F. A. FUHRMAN (U.S.A.) described the pattern of electrolyte and carbohydrate changes in tissues (mainly muscle) injured

by anoxia. He showed that the electrolyte changes fell into four groups according to whether the pattern remained unaltered, whether there was a simple increase in the extracellular space, whether there was cation shift with a normal or large intracellular volume, or whether there was a cation shift with a small intracellular volume.

J. TREMOLIÈRE and R. DERACHE (France) described the effect of injury on the organic phosphates of the damaged tissues. While the pathway of the breakdown of adenine nucleotides in ischæmic muscle with their accumulation as inosine monophosphate and subsequent release from the damaged muscle in this form was now well known, there was need for further work on the changes in the phospholipid and nucleic-acid fractions.

General Response to Injury

A. FONNESU (Italy) regarded " cloudy swelling " as an early cellular response to injury, and described work from his laboratory supporting the view that this change was due to an alteration in the mitochondria leading to an " uncoupling " of oxidative phosphorylation, increased glycolysis, and at the same time increased protein synthesis.

H. B. STONER and C. J. THRELFALL discussed the question of the degree to which the effects of injury, particularly those on energy and carbohydrate metabolism, could be explained by tissue anoxia. They showed that in tourniquet shock in animals there was a period, shortly after removal of the tourniquets, when distinct biochemical changes were occurring despite adequate oxygenation. They ascribed to anoxia the changes in the later part of the survival period.

A. G. B. KOVACH (Hungary) described the work of his group on the effects of hæmorrhage and limb ischæmia on the biochemistry and physiology of the central nervous system. The impaired function of the central nervous system was thought to play an important part in the development of the general response to injury.

R. FÅHRAEUS (Sweden) discussed the increased tendency of the erythrocytes to aggregate after tissue injury and showed how this could affect the oxygen supply to the tissues.

V. WYNN emphasised the effect of injury on the ability of the body to control the distribution and excretion of water. In the past insufficient attention has been paid to the changes in water metabolism after injury.

The important effects of changes in environmental temperature on the lethality of an injury and on the biochemical changes which accompany it were described by R. E. HAIST (Canada), who also discussed the trauma-resistance of the cold-acclimatised animal.

Bacterial Factors in Response to Physical Injury

H. SMITH (England) showed how bacterial infections themselves could lead to a state very similar to that produced by physical injury. In some cases (anthrax) this was due to loss of fluid from the vascular system, but in others the mechanism was more obscure.

W. W. SPINK (U.S.A.) also described the metabolic and physiological responses to infection—in this case by brucellæ—and included a discussion of its effect on the adrenal cortex.

J. FINE (U.S.A.) described the evidence acquired by his group in support of the view that the action of bacterial endotoxin is the reason for the development of the irreversibility to transfusion of hæmorrhagic shock. He suggested that impairment of the ability of the reticuloendothelial system to neutralise endotoxin could decide the outcome in hæmorrhagic shock.

The proceedings will be published by Blackwell Scientific Publications.

GERONTOLOGY

FROM A CORRESPONDENT

THE European clinical section of the International Association of Gerontology held its first conference last week under the able chairmanship of Dr. J. A. HUET (France); and the choice of Sunderland for this very successful meeting was at once a tribute to the late Oscar Olbrich and an acknowledgement of the remarkable growth of the hospital geriatric service in this country. Those who maintain that there is no justification for such a specialty forget that geriatric medicine had its origins in the needs of a piteous multitude of sick elderly people: needs so clamant that, here, the planners of a National Health Service were obliged to create hospital geriatric units to meet them; and the success of these units continues to determine the creation of new ones. The first task of geriatrics was to concentrate on social aspects, on organisation, and on the new found arts of restoring mobility. But with the appointment of many new consultants, most with wide medical backgrounds, it was inevitable that it should look further and encompass the endless variations of disease in the elderly. At Sunderland a more precise definition was given to some aspects of clinical geriatrics; but it was more important that the geriatric physician and the expert in adjacent, or overlapping, clinical and experimental fields should have met so happily and with such mutual benefit; for that, as Olbrich realised, is the pattern of good hospital geriatric practice. The " multiple pathology " of the elderly, and the opportunities for therapy, are more than any one person can know, and the physician will best serve his patients by consulting freely with his colleagues. They, in turn, will draw from his knowledge of the home background and from his wider experience of old people and their illnesses.

A recurring theme at the conference was that old age per se was seldom a bar to necessary investigation or treatment: contraindications were those that applied at any age. Thus, for Prof. E. GREPPI (Italy), the president of the Association, and Prof. B. PRUSIK (Czechoslovakia), anticoagulant therapy carried no special risk in well-chosen elderly patients. In chronic urinary infections a patient's age would not deter Dr. TORBEN GEILL (Denmark) from a thorough search for surgical lesions of the urinary tract; and Mr. HAMILTON ROSS (Sunderland) considered that the dangers of prostatectomy in the octogenarian had been overstated. In the best hands, and with skilled preoperative and postoperative care, the mortality was little over 10%. Most would agree that this is a small risk when set again the miseries of permanent suprapubic drainage. Dr. STEN ECKERSTROM (Sweden), Dr. L. E. TOTTERMAN (Finland), and Dr. O. TAYLOR BROWN (Dundee) dealt with the still-vexed question of urinary incontinence. Most cases were associated with a spastic hyperexcitable bladder, the result of a neurological disorder. A few successes may follow the treatment of local conditions and infections; or ambulation and habit retraining; or the repeated use of cystometric methods. But little permanent improvement is to be expected in the presence of dementia.

The conference devoted much time to the discussion of confused states. Prof. MARTIN ROTH (Newcastle) asked for clear definition of the various disorders, particularly delirium, dementia, and depression, with their different implications for prognosis and therapy. In cases of delirium Dr. F. J. FLINT (Sheffield) illustrated the high

incidence and great variety of metabolic disorders and organic mischief in the various bodily systems. Giving a graphic description of the delirious state, Prof. A. KENNEDY (Edinburgh) advocated that nursing care should be designed to induce a sense of security and of continuity of place, time, and person. In the matter of sedation Dr. THOMAS RUDD (Southampton) preferred to avoid giving sedatives to confused old people until attempts had been made to relieve bodily discomfort in other ways; he quoted Evans' remark that mersalyl was the best sedative in congestive cardiac failure. Barbiturates and bromides should be avoided altogether: safe sedatives for the elderly were chloral, dichloralphenazone, phthalimidoglutarimide, methylpentynol, and alcohol, with paraldehyde in reserve if something stronger was needed.

Public Health

Poliomyelitis Vaccination

THE Minister of Health last week launched a drive to raise the number of children under 15 vaccinated against poliomyelitis, of whom only about half have so far been registered. By the end of August the number of children up to the age of 15 who had been registered in Great Britain was 6,800,000 (56% of those eligible in this age-group). Just over 5,600,000 of them had received two injections and over 410,000 one injection.

In a message to parents, the Minister said that " this summer we have had the fewest polio cases in the last ten years. This is very good and we can all be thankful. But it is not too soon to be thinking about next year, if we are going to be certain of keeping polio down to a minimum then. We know that in the past the incidence of polio has fluctuated dramatically from year to year. Next year may be one of Nature's heavy polio years. And therefore we must build up all the defences we can against it."

By the end of September over $17\frac{1}{2}$ million doses of vaccine, of which nearly $10\frac{1}{2}$ million were Salk, had been distributed to local health authorities in Great Britain. Supplies of British-produced vaccine are still limited, and parents are strongly recommended by the Ministry to avoid delay by accepting whatever vaccine is available locally.

Infectious Diseases in England and Wales

Disease	Week ended September 6	13	20	27*
Diphtheria	3	3	2	2
Dysentery	316	329	410	433
Encephalitis:				
Infective	1	2	5	3
Post-infectious	3	..	1	1
Food-poisoning	275	302	369	347
Measles, excluding rubella	1979	1606	1470	1621
Meningococcal infection	10	16	9	10
Ophthalmia neonatorum	22	48	17	25
Paratyphoid fever	9	4	5	5
Pneumonia, primary or influenzal	144	145	175	154
Poliomyelitis:				
Paralytic	60	40	48	54
Non-paralytic	20	22	31	41
Puerperal pyrexia	188	206	226	221
Scarlet fever	305	298	434	543
Smallpox	..	..	..	..
Tuberculosis:				
Respiratory	414	500	458	465
Meninges and C.N.S.	11	8	6	7
Other	62	61	56	59
Typhoid fever	5	2	6	6
Whooping-cough	791	761	718	671

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

I LOOKED up and saw the coloured bus-conductor, so, things being as they are and as I have vague feelings of being a broad-minded chap, I said " please " a bit louder than I usually do, and " thank you " when I got my change and again when I got my ticket. I must admit, cosily reading my paper, I felt just a little bit good. Suddenly I realised that the bus was filling and that everyone was " pleasing " and " thankyouing " with unusual emphasis. Then I noticed that our driver was also coloured. " They're good at cricket," I thought to myself, " so he's probably a pretty good driver." But he wasn't, at least not particularly, and we were all thrown about rather more than I like. " Lots of English drivers are below par ", I thought to myself, and, when another man said jovially " He'll have the money out of our pockets in a minute " everyone seemed to read just a little harder. However, the restoration of international relations wasn't one-sided. A pleasant, middle-aged lady asked where a road near Hyde Park Corner was which I imagine we all knew. We were silent, of course, while our conductor paged through his *A1 Guide*. It was a long job, but no-one dreamed of interfering. He was still shouting directions to her as she crossed the road going in the wrong direction. I went on feeling good all the way to the hospital.

* * *

One of the great advantages of a caravan for the family holiday is the ease with which you can make overnight stops. This gives you a wonderful sense of freedom in that you can take as long as you like over the journey. I find that the average farmer is most cooperative about camping on his land, provided one behaves oneself and disposes of the rubbish in a decent manner. It is the tins that cause the most difficulty: the only way is to bury them.

This year we hired a caravan and went to Arisaig, taking four days to get there and three to return. The last thirty miles —along the famous Road to the Isles—were a problem: the humps on the road are sometimes so acute that you have to take them diagonally in order to see over your own bonnet. Our memory of this stretch on the outward journey was so vivid that, when we had negotiated it on the homeward run, we thought all our difficulties were behind us. It was farther on, on the circuit of Loch Leven—and miles from anywhere, of course—that one of the caravan tyres punctured. Our car has automatic jacks, but I had noticed, rather idly, that there was a jack in the caravan: what I had not realised was that it had no handle.

We did the only thing possible: unhitched the caravan and, leaving it perilously near a corner, went off in the car to borrow a jack. It took four 10-mile journeys before we had everything fixed up, and by this time it was dusk. We had asked the garage man about a site for the night, and he had said it would be all right to go on the foreshore by the road junction at Glencoe village, and that there was no question of payment to anyone. So we nosed our way, with the light of a torch, on to what seemed to be a nice, flat site, and went to bed.

No wonder there was nothing to pay. We wakened to the discovery that we were on the public rubbish dump. For once, the disposal of our empty tins gave no trouble at all.

* * *

Dawn cracks a little later for me than for the rest, and I do not leap easily out of bed; nor do I do exercises before breakfast; but I do get up and shave and dress and manage to sit up at the table whilst eating.

While the various internal adjustments to the upright posture proceed I am not too quick mentally and may appear abstracted or even gaga to the uninitiated, but usually of course the uninitiated are not there. Unseen, however, the unconscious is quietly giving birth to consciousness, and it is at this time that my mind is most easily influenced. Thus outward appearances are dangerously deceptive. Minor environmental stresses such as a query as to whether I could pass the salt at this time may have violent repercussions. It is not that the

particular stress is of any import, but that any outside stimulus, if too violent, may precipitate the arrival of consciousness—premature and angry. There are no hard and fast rules about what is safe and what is unsafe to say. What passes off normally one morning may prove immediately fatal on another. And again a rude awakening may one day reveal a buoyant happy self whereas on another day it discloses a raving maniac.

I would not describe myself as temperamental or even excessively extraverted. In fact I am a rather cold and logical sort of person. It is just, I suppose, that I do not adapt myself easily to sudden changes, and the change from the horizontal to the perpendicular, from night to day, from bed to breakfast, is too much for me.

* * *

For some obscure reason everyone assumes that because I am in public health my only interest is drains. The laity and the clergy I can forgive, but my colleagues are breaking my heart. As soon as I join a group at the local clinical meetings the discussion of interesting cases, rare complications, and strange sequelæ fades away, and after a suitable pause the talk turns to chemical closets. And no matter how I try, I never seem to be able to raise it again above knee-level.

Last year I represented my specialty on a Scandinavian tour. When everyone else was shown the wards, I was shown the lavatory systems. Even in Copenhagen, that centre of understanding, it was only as a special favour and after much pleading that I was allowed to see a chest clinic instead of the municipal sewage farm.

But I must admit I have my moments. Only last week one of our most distinguished clinicians, a man of international renown, called me in in consultation. He needed my advice badly, and he admitted quite frankly that I was the only one to whom he could turn. His front drain was blocked, overflowing, and odoriferous; could I arrange for its speedy repair?

Even at home I am not immune. When I returned from work the other evening, my wife pointed to our little John. "He's ill," she said distractedly, "I think he has a fever." To me it was simply his first tooth, but it was obvious that my explanations were not being received as wholeheartedly as they might. Even the use of my stethoscope, produced dramatically from the kit which I use to teach first-aid, failed to convince her. "I'm sorry, dear," she said, "but I'm going to call a real doctor." I must have shown my chagrin, for she continued, not unkindly, "While we're waiting you might fix the you-know-what. It's not working right, and you do it so much better than the plumber." Well, I must admit I do have rather a knack with them, and besides, when you get down to it, they are jolly interesting.

* * *

Disposing of the body, my old nurse always used to say, was the nub of a successful murder; but I've solved all that. I shall lure my victim to a Brittany *plage* in September, commit the crime on Oct. 1, and, however carelessly the corpse is left about, there will be no one to find it until at least the following May or June. This year the *rentrée* was earlier and more complete even than usual as everyone went home on the 27th in order to let de Gaulle have his *oui* on the 28th. Of course I'm not referring to *plages* which have a hard core of rural or fishing life, but to the pure artefacts, like St.—— and Les Sables——. The shop windows are papered with yellowing newspapers, those hotels which are not up for sale as flats—surely a sign of the times?—are boarded up, and the silence and desolation are complete, but complete. No cat barks. It was, therefore, surprising at one such St. Sahara-sur-mer to find on the sands, smooth and shining from the falling tide, a circle of tracks about six feet across as if two dogs had been fighting or enjoying a playful scuffle. Thirty yards on were similar marks, but there were no tracks, human or animal, approaching the circles or joining them. My wife suggested cats, huge grey ones, going to some *fin de saison* witches' coven in thirty-yard bounds or on a jet-powered broomstick that had run out of fuel. A little far-fetched perhaps, but can anyone suggest a better explanation?

Letters to the Editor

GALEN IN CHINA

SIR,—I was interested to read Professor Gould's interpretation (Sept. 20) of the fostered coexistence in China of modern medicine with the traditional arts of healing. He explains this to be mainly due to political reasons—namely, the fear of the Communist Government that its power would be undermined if the doctors were to be taught modern scientific medicine only.

I wonder whether he feels that the same explanation applies to the official encouragement which the traditional "schools" of healing get in India or Ghana, where the governments in power are not Communist. When I first encountered this phenomenon during my work in India—and was shocked by it as Professor Gould is—I came to the conclusion that the main motive was one of economy. After all is said and done the doctors in the Western countries treat a large number of their patients by placebos—with or sometimes without insight. The large-scale dispensation of the "tranquillisers" and sedatives is not "scientifically" superior for all the pseudoscientific garb with which they are being marketed—very often after controlled trials have shown them to be useless. These drugs which are used as placebos, however, are expensive, and the underdeveloped countries cannot afford them in large quantities. The traditional remedies are infinitely cheaper, and as placebos go home better because they are rooted in the native beliefs and customs. The Indian medical practitioner does not do any worse for his patients if he prescribes a traditional herb instead of a tranquilliser. Sometimes the herbal teas or local applications which the indigenous medical men use, like many of the remedies which are known to village folk in European countries, contain a therapeutically active ingredient. Once such a concession is made to the traditional "schools", however, there are always fanatics in traditionalism both in and out of Government who spread their sails before this wind. Could this apply to the situation Professor Gould found in China?

The Indian or African practitioners often claim that these older forms of treatment are "scientific". This is a wrong use of the term scientific. What they in fact mean is that, whatever the explanation for the mode of actions of their remedies, *empirically* they have been found to be of value. The only way of testing this would be to conduct controlled treatment trials. The doctors trained only in the traditional schools will never undertake that, because their training does not make them see the need of it. If, however, scientifically trained doctors are encouraged to study these old teachings, their approach might help to sort out what is useful from the rest. It should not be overlooked that drugs like quinine, morphine, and reserpine were contained in those old pharmacopœias as empirical treatments long before they came to be investigated by scientific methods.

As long as these countries still depend for the major part of their medical services on the indigenous "doctors" because they are much cheaper to train, it will in the long run be better in every way if the doctors trained along modern lines are encouraged to study these old teachings, rather than ignore them.

Apologia: I fear my tentative explanation is less imaginative than Professor Gould's, but do his sinister insinuations really help anyone? To us, as he himself

suspects, they sound farfetched; to the doctors who work in the underdeveloped countries with their enormous problems they must sound rather silly.

Department of Psychiatry,
The Royal Infirmary,
Manchester.
J. HOENIG.

CONTROL OF THE COMMON COLD

SIR,—I have read Dr. Ritchie's letter of Sept. 27 with much interest. When it appeared I had in draft a letter describing my own attainment of immunity from common colds, from which I have just completed three years' freedom. Repeated infections or reinfections have invariably aborted without discomfort in 2–5 days, including my annual September one, the result of which I waited for before writing to you.

During the 4 years September, 1951, to August, 1955, I had three fully developed colds, two of which were used for immunisation purposes. Previous to this I had had regularly at least two or three full colds a year, always one in September or early October, each accompanied by marked coryza and general malaise and followed by a long severe purulent bacterial stage usually with loss of voice and much coughing at nights. Adequate doses of penicillin, however, rapidly terminated the second stage. Stock and autogenous vaccines had had little effect on the incidence or course of my colds.

About 8 years ago, during my early "autumnal" cold, circumstances made it necessary for me to avoid the long secondary stage if possible and I started penicillin treatment early in the bacterial phase. The secondary phase was completely aborted but to my surprise the cold was "let loose" and for the next two weeks I had a severe cold with all the usual accompaniments (coryza, malaise, headaches, &c.) but not followed by a bacterial phase. This was followed by a period of relative immunity, for the next cold (some six months later) aborted, a most unusual experience. I concluded that the effect of the bacterial phase of a cold was to lock up the cold virus and arrest or limit its general spread and so prevent its giving rise to any immunising reactions.

I therefore decided that at the next cold I would try a combination of penicillin followed by an autogenous vaccine prepared from the preponderant organisms (*Streptococcus viridans*, *Str. pyogenes*, and *Neisseria catarrhalis*, all penicillin-sensitive) cultured from swabs taken at the beginning of the secondary stage, which was then terminated with penicillin. I waited till the next cold started (in September, 1951), which I recognised from previous experience was likely to be of the usual severity, and at once on the first day started penicillin medication. The cold lasted about two weeks with marked general effects, but no bacterial phase. On recovery, I started graded doses of the vaccine extending over the next 10–12 weeks. This was followed by a period of about 15 months during which colds aborted, and then ended by a full cold as before.

I repeated the penicillin and vaccine treatment on a cold beginning in September, 1953, with rather better results, and again in September, 1955, when a new vaccine was prepared from swabs taken early in the bacterial phase. Since then repeated reinfections have aborted in 2–5 days and during the past 3 years I have not had a full cold develop or a bacterial phase. I have had two other apparently virus infections, both without coryza, one a mild influenzal type during an epidemic, and one described as "virus laryngitis"; neither had a bacterial stage.

The vaccines I used were prepared from organisms isolated in pure culture in the usual way and killed by storing at 0–4°C in 0·5% aqueous phenol. I am grateful to my colleagues for preparing them. In the third course, which extended over 4 months, the final doses reached high levels (up to a total of 8000×10^8 organisms per dose).

I am satisfied, especially after reading Dr. Ritchie's letter, that the procedure I have followed has given me immunity, this not being due to accident or increasing age. It appears that repetition of the process of auto-immunisation by penicillin treatment and of immunisation by vaccine is necessary to build up a prolonged immunity.

West Park Hospital,
Epsom, Surrey.
W. W. KAY.

TRIPLET PREGNANCY WITH CONJOINED TWINS

SIR,—I was most interested to read the article by Dr. Franklin and his colleagues (Sept. 27) wherein is described a case of craniopagus twins associated with a third normal fœtus in a triplet pregnancy. The description as "unique" of the occurrence of conjoined twins in a triplet pregnancy is, however, far from correct. In fact I believe the reverse to be true—namely, that conjoined twins are more common in triplet pregnancy. To my knowledge, in the last 10 years three such pregnancies have been described. Foster [1] reported a male thoracopagus following a normal female fœtus; Jorgensen [2] reported a case in which the single fœtus followed the thoracopagus; and Mazumdar [3] reported a male syncephalic thoracopagus monster which had been preceded by a single normal male fœtus.

There is little literature on the obstetric aspects of conjoined twins and to have encountered relatively recently three cases of conjoined twins in triplet pregnancy indicates, I believe, that, whatever the cause of this unfortunate union of fœtuses, it is particularly operative in triplet pregnancies.

I might add that Adair [4] cites a case occurring in a quadruplet pregnancy.

Ipswich. HUJOHN RIPMAN.

MECAMYLAMINE AND THE NERVOUS SYSTEM

SIR,—Dr. Hickish's letter (Oct. 4) spotlights the increasing number of reports of untoward neuromuscular signs following administration of mecamylamine. We have recently had a case of mecamylamine toxicity following closely after potentiation of the drug by chlorothiazide.

The patient, a woman of 48, was admitted to hospital in August, 1957, in cardiac failure secondary to hypertension. Blood-pressure was 260/170 mm. Hg and the fundus revealed papillœdema, exudates, and hæmorrhages. After full investigation a diagnosis of essential hypertension was made.

Treatment began with mecamylamine (20 mg. b.d.). After one month's inpatient treatment the blood-pressure had been reduced to 120/80 and fundal changes were reversing. Although the fundi reverted to normal after discharge from hospital, the blood-pressure began to rise once more. The dose of mecamylamine was slowly increased and reserpine added. By early July, 1958, the patient was receiving mecamylamine 80 mg. per day and reserpine 0·75 mg. per day, both in divided doses. In spite of restriction of activity the blood-pressure was 260/125.

During July and August fundal changes again developed and, rather than further increase the dose of mecamylamine, chlorothiazide (0·25 mg. b.d.) was prescribed.

About fourteen days later the patient noticed an uncontrollable tremor which increased in severity over the next fortnight before she returned to the outpatient department. She had a generalised coarse compound tremor which at times was sufficiently severe to suggest a rigor. It was present at rest, but was exaggerated by voluntary movement. There were no pyramidal, cerebellar, or sensory signs. Blood-pressure was 280/140 and there was evidence of early cardiac failure. The patient was naturally anxious but not psychotic.

After admission to hospital and withdrawal of both meca-

1. Foster, P. M. *Amer. J. Obstet. Gynec.* 1948, **56**, 799.
2. Jorgensen, G. *Ugeskr. Laeg.* 1954, **116**, 208.
3. Mazumdar, L. B. *J. Indian med. Ass.* 1956, **26**, 313.
4. Adair, F. L. *Amer. J. Obstet. Gynec.* 1930, **20**, 539.

mylamine and chlorothiazide the tremor rapidly diminished, although it was still detectable ten days after withdrawal.

The addition of chlorothiazide did not appear to potentiate the hypotensive effects of mecamylamine, but it may have facilitated the appearance of an untoward reaction to this drug.

I am grateful to Dr. T. D. Kellock for permission to report this case.

Central Middlesex Hospital, London, N.W.10. A. M. CONNELL.

BLANKETS AND INFECTION

SIR,—Your issue of Oct. 4 contains many views on hospital bedding. All are very interesting and show an awakening interest in this subject.

Taken as an economic proposition, most hospitals have a great store (in hospital beds) of blankets. To replace them all at once would be very costly. As the woollen blankets wear out, new ones can be made of other materials. The process of replacement must necessarily be slow, and in the meantime cross-infection must be prevented. We have found that a most effective process consists in the routine of dirt removal by 'Lissapol' (which also removes traces of soap which might neutralise the activity of the next-stage chemical) followed by thorough rinsing and partial drying in a centrifuge (spin-dryer) preparatory to soaking for twenty minutes in 'Fixanol C', and then complete drying, without further rinsing. The blankets are not damaged and the fibres adsorb some of the quaternary ammonium compound, and retain their antibacterial properties for four weeks. In our experience 'Cirrasol O D', although much vaunted, is inferior to fixanol C.

Although the lissapol and fixanol C routine is very satisfactory from the viewpoint of the prevention of cross-infection, the procedure involves much manual labour; and labour is very costly.

For some years we have been looking for a means of reducing these labour costs. We had in mind a chemical which would combine the operations of "cleansing" and "sterilisation" in one process. Until quite recently we were unsuccessful in our search. A few weeks ago we gave a trial to blanket washing and sterilising—in one operation—with 'Hytox', a proprietary preparation marketed by Domestos. Hytox has now been tried at one of our hospitals with great success. The blankets emerge very white, soft, and clean, and the fibres have antibacterial properties and are sterile. Hytox also is inactivated by traces of ordinary washing-soap in the blanket or in the crevices of the washing-machine; so the first time a used blanket is washed the results may be disappointing. However, the second time the blankets are washed in a clean machine the results are very satisfactory.

St. Margaret's Hospital, Epping, Essex. FRANK MARSH.

ORAL TREATMENT OF PERNICIOUS ANÆMIA

SIR,—We judge from the reply of Dr. Mooney and Dr. Heathcote (Aug. 16) to Professor Castle's comments (Aug. 2) on their recent article [1] that they are unwilling to accept certain data which, in our opinion, completely invalidate their conclusions with respect to their "vita-[1]min-B_{12}-peptide complex".

The fundamental criticism remains that their study lacked controls: they failed to use patients who were to receive only vitamin B_{12} without the peptide or any other additives. This lack of a control makes any conclusions untenable. Many studies [2–7] have shown that small oral amounts of vitamin B_{12}, from 5 μg. to 100 μg. daily, will often produce remission in patients with pernicious anæmia in relapse. 11 consecutive patients in one study [4] received 5–15 μg. of vitamin B_{12} by mouth daily for five months; there was an almost regular occurrence of remission, with 3 of the patients showing a maximal response. All this, it must be noted, was without added peptide or any other substance.

There are two mechanisms of vitamin-B_{12} absorption,[8 9] one of which is intrinsic-factor-dependent, and the other independent of intrinsic factor. It is this latter mechanism which is primarily responsible for the absorption of significant amounts of vitamin B_{12} when oral doses in excess of 2 μg. are ingested.

There is the slight possibility that a peptide may stimulate gastric secretion of the slight residual intrinsic factor still present in some patients with pernicious anæmia,[10] in a manner similar to carbachol,[11] and perhaps *d*-sorbitol.[12]

Their comments with respect to the existence of intrinsic factor are pure speculations, unrelated either to their own studies or the many studies on which the concept of existence of Castle's intrinsic factor firmly rests.

VICTOR HERBERT
SOLOMON ESTREN
EUGENE BRODY
LOUIS R. WASSERMAN.
Mount Sinai Hospital, New York.

WATER FLUORIDATION

SIR,—I am rather surprised at the attitude taken by your correspondent (Oct. 4, p. 741).

A few facts are essential for consideration.

(1) Waters containing fluorides at 1 part per million do not taste, smell, or appear different from that with a trace.

(2) All waters in this country, so far as I know, contain some fluoride.

(3) Water treatment often causes a slight reduction in the fluoride level.

(4) Populations living in areas containing fluoride at levels of 2, 3, or more parts per million do not suffer from ill health or disease.

(5) The amount of suffering in children which is avoidable is immense.

(6) The ordinary person's attitude (and having discussed this with a considerable number of members of the public I think I know their attitude) is that he is all for it if aware of the facts.

(7) If some members of the public have been frightened by a thoroughly dishonest campaign then they are against it.

(8) The "freedom of choice" argument also applies to chlorination and all aspects of water treatment.

(9) The lies and half-truths put out by the opposition would not be used if there was a genuine case. The methods used have been exposed in the New Zealand report.

(10) I am surprised, indeed amazed, that your correspondent suggests that the public (mothers of 8 children included!) would administer fluoride tablets. Does he know that this would have to be done for years and years and years? Most patients have difficulty in persisting with any treatment lasting for more than a few days.

(11) Is your correspondent aware of the present accident-rate from children taking tablets in the home?

(12) If those who want lower fluoride water (e.g., the more usual 0·2 p.p.m.) live in a fluoride area, they can install a defluoridator. After all, I prefer private education for my child, so I pay for it. If there is a demand for defluoridators they will, doubtless, be produced by private enterprise for the few who want them.

It is, Sir, I know, possible to get a Council to approve fluoridation without contrary votes. It does take a lot of

1. Heathcote, J. G., Mooney, F. S. *Lancet*, 1958, i, 982.
2. Estren, S., Wasserman, L. R. *Proc. Soc. exp. Biol., N.Y.* 1956, **91**, 499.
3. Hall, B. E. *Brit. med. J.* 1950, ii, 585.
4. Glass, G. B. J., Boyd, L. J. *Blood*, 1953, **8**, 867.
5. Glass, G. B. J., Boyd, L. J., Rubinstein, M. A., Svigals, C. S. *Science*, 1952, **115**, 101.
6. Chalmers, J. N. M., Hall, Z. M. *Brit. med. J.* 1954, i, 1179.
7. Ungley, C. C. *ibid.* 1950, ii, 905.
8. Ross, G. I. M., Mollin, D. L., Cox, E. V., Ungley, C. C. *Blood*, 1954, **9**, 473.
9. Doscherholmen, A., Hagen, P. S. *J. clin. Invest.* 1957, **36**, 1551.
10. Goldhamer, S. M. *Amer. J. med. Sci.* 1936, **191**, 405.
11. Mollin, D. L., Booth, C. C., Baker, S. J. *Brit. J. Hæmat.* 1957, **3**, 412.
12. Herbert, V. *Amer. J. clin. Nutr.* 1958, **6**, 547.

hard work and energy. As we are usually ruled by a party with not much more than half the country behind them I think further comment is superfluous.

Public Health Department,
Bedford. C. L. SHARP.

INTERNATIONAL SOCIETY FOR CLINICAL AND EXPERIMENTAL HYPNOSIS

SIR,—In view of the past vicissitudes in the practice of hypnosis and its present revival, it may be of interest to your readers to know the latest organised developments in this field. On Oct. 5 the International Society for Clinical and Experimental Hypnosis was inaugurated.

This is a society which has branches in this country, the U.S.A., Argentina, Australia, Brazil, Canada, Chile, Denmark, Germany, Japan, the Netherlands, Norway, Sweden, and South Africa. Branches are also being formed in France and Italy at the present moment. The British section of this society contains 124 members, and a journal, the *International Journal of Clinical and Experimental Hypnosis*, is published quarterly. The Society consists of medical practitioners, dental practitioners, and psychologists and is divided into fellows, members, and associate members. An American board of examiners in clinical hypnosis has been formed with medical, dental, and psychology divisions. This board is patterned after the other certification boards of the American Medical Association.

As, for so long, the practice of hypnosis has been sporadic, and any real value it might have overlaid and distorted by exaggerated and wishful claims, which were rarely followed up, the formation of this group is a major step forward to allow hypnotism to take a reasonable place beside other therapies.

The aims of the group, apart from teaching and the exchange of knowledge on the subject, will be greatly concerned with a scientific and unprejudiced assessment of its true value. The preponderance on the board of directors of the society of many eminent experimental psychologists and psychiatrists from the major American hospitals should make this aim realisable.

A. A. MASON
Secretary, British Division
of the International Society for
Clinical and Experimental Hypnosis.
37, Devonshire Place,
London, W.1.

PSYCHOLOGY OF LABORATORY ANIMALS

SIR,—Dr. Watson (Oct. 4) takes exception to a statement contained in the article which you kindly published (Sept. 20, p. 632) on the work of UFAW—namely, that UFAW is "inaugurating a long overdue study of the psychology of laboratory animals". Nevertheless this statement is true if rightly understood. Naturally nobody who is interested in the subject can be unfamiliar with Munn's book, to which Dr. Watson refers, or with at least some of the subsequent work on rats. Vast numbers of observations have, indeed, been made on the reactions of rats to various artificial situations chosen for the convenience of the observer, and many of these have yielded knowledge which is interesting or useful to humans. But it is of precious little use to rats (which, in my humble opinion, are of all laboratory animals the most lovable and perhaps the most in need of compassion).

What UFAW is inaugurating is a study, for the benefit of the animals themselves, of their psychology under the conditions which laboratory conventions have provided for them but which may, for all that is at present known, be far from optimal from the animals' point of view. An example will illustrate the point. In the course of an assay in which the weight of the ovaries was the criterion, Chance found that when female rats were solitary in their cages the results showed an enormous variance, whereas when each rat had one female cage-mate a sensational reduction in variance was obtained. Could all Munn's army of mazologists have predicted this curious psychosomatic effect? It may well turn out to be only one of a number of hitherto unnoticed factors affecting the mental comfort of laboratory animals.

C. W. HUME
Secretary-General,
Universities Federation for Animal Welfare.

MINAMATA DISEASE

SIR,—Dr. Meiklejohn suggests (Oct. 4) that a natural poison (antithiaminase) in fish caught in Minamata Bay may have been the cause of the outbreak we described (Sept. 20). We considered this possibility in view of the association of a peripheral neuritis and deafness in many of those affected, since this combination of symptoms may occur in deficiency states. However, for the following reasons this explanation seemed to us untenable.

(1) The eating of raw fish, more particularly by fishermen and their families, is customary throughout Japan; yet, as far as we could ascertain, no similar outbreak has previously been reported.

(2) Antithiaminase is found in certain varieties of *fresh*-water fish and in shellfish. In the majority of the affected families the amount of shellfish consumed was negligible as compared with other varieties of sea fish.

(3) Cooked as well as raw fish appeared to cause the disease. As Dr. Meiklejohn points out, antithiaminase is destroyed by cooking.

(4) The fish in the bay were themselves affected, suggesting the action of an extrinsic poison.

(5) The characteristic cerebellar picture shown by these patients, due to neuronal degeneration of the granular layer of the cerebellum, has not been described in any of the nutritional disorders of the nervous system.

Dr. Halstead, a member of an institute for the study of fish-poisoning in California, has recently visited Minamata, on behalf of the Institute of Neurological Diseases and Blindness, Bethesda, Maryland. The results of his chemical analysis of fish, shellfish, sea water, and effluent from the bay may throw further light on the nature of the toxic substance responsible for the outbreak.

The Institute of Clinical Research,
The Middlesex Hospital Medical School,
London, W.1. DOUGLAS MCALPINE.

TREATMENT OF BREAST CANCER

SIR,—The "devil's own question", as Dr. Berkson and his colleagues (Sept. 6) described the problem of comparability of cases of breast cancer, seems to call for an answer—despite the fact than *an* answer, drawn from all fields, has already been put forward repeatedly. Even from one angle the answer comes fairly clear. In large part, it is provided by the difference between the proportions that stage-I forms of various series of breast cancer. Berkson et al. point out that the Mayo Clinic deals more than some clinics with referred cases, often from a distance, and local doctors tend to refer only their advanced cases to the "court of last resort". It might be expected, therefore, that the Mayo Clinic cases would have a smaller proportion of stage-I than would those of other clinics. But stage I formed no less than about 50% of a whole series recently reported by this clinic, while it formed only 11% of a whole series of about the same time reported from the Toronto General Hospital.[1]

Such large difference is perhaps the extreme and smaller differences are more usual. However, it serves

1. *Canad. med. Ass. J.* 1958, **78**, 781.

best to illustrate, I think, a wide range of selection through diagnosis—not deliberate selection. As Budd said, in 1867, in reference to his contention that tuberculosis is an infectious disease, " Try every other supposition, and the facts are inexplicable; make this one supposition, and they are at once explained ". Such selection through diagnosis renders generally invalid and misleading the comparison of survival-rates of series of different times or places, or of series in which the diagnoses were made, or rather " proven " (!), on different criteria—death from breast cancer or clinical findings with or without microscopy.

Department of Epidemiology and Biometrics,
School of Hygiene,
University of Toronto. N. E. McKINNON.

TREATMENT OF HYPERPYREXIA

SIR,—A hyperpyrexia which lasted some six hours before responding to treatment is reported by Dr. Johnston and his colleagues (Sept. 27). It seems desirable to bring very high temperatures down as soon as possible, although it is often difficult to know how much the symptoms and sequelæ in a case are due to the hyperpyrexia rather than to the underlying brain disorder.

Intragastric cooling [1] is simple and deserves to be used as a symptomatic treatment for hyperpyrexia as soon as it is evident that cooling by external sponging and fanning is not bringing the temperature down from what are probably dangerous levels.

The apparatus is simple; a finger stall or a condom tied firmly on to a 'Polythene' tube and a 50 ml. syringe are all that are needed. The balloon is passed into the stomach, and cold water from a container of water with melting ice is squirted down the tube, sucked out, and replaced with more cold water. In a child hyperpyrexia was ended in half an hour.

Elaborations of the technique with inflow and outflow tubes and continuous perfusion machines have been described by Barnard,[2] and more recently by Khalil.[3] Experience with the technique [2 4 5] suggests that it is simple and safe, and that the reduction of temperature is easily controlled. It has proved valuable for cardiac surgery [2] and for brain surgery.[3]

In hospitals and sick bays in hot climates it might be worth while having a continuous perfusion apparatus for treatment of hyperpyrexia which fails to respond quickly to cold sponging.

London, S.W.1. R. C. MAC KEITH.

CHLORPROPAMIDE

SIR,—Following the account by Dr. Murray and his colleagues (Sept. 13) of trials with chlorpropamide, Dr. Walker (Sept. 20) gave her experiences in treating a group of 43 diabetics with this new oral hypoglycæmic drug. She found that " nausea, anorexia, and vomiting were unpleasant " in over a third of her patients, and in 9 of these vertigo was severe with demonstrable nystagmus.

We have now treated 41 diabetic patients with chlorpropamide, and our experience as to its toxicity runs somewhat counter to that of Dr. Walker's.

In the main, on a daily dose of 500 mg. or 200 mg., we have found the drug has been well tolerated by most patients. We have had no complaints of nausea, anorexia, or giddiness. In 2 of our patients, a generalised rash developed within a week of starting treatment, suggesting a sensitivity reaction: the rash faded when the drug was discontinued. An elderly patient treated with 1 g. a day (a higher dose than we now employ) became confused and febrile with a generalised rash; some of these symptoms may have been due to a concurrent pneumonia. 2 patients developed diarrhœa soon after taking the tablets, but in each case other causes for the diarrhœa were present. We have found no evidence of toxicity either in the blood or in the liver-function tests.

On the whole, chlorpropamide seems more effective than tolbutamide and has a longer action, so it need only be given once daily. These are real advantages, and if the drug is well tolerated it is certainly worth further trial. In the main, our experiences are very similar to those of Dr. Murray and his colleagues, and we are continuing to use these tablets with patients under close supervision.

K. L. GRANVILLE-GROSSMAN
SUSANNE CRAWFURD
Whittington Hospital, ARNOLD BLOOM.
London, N.19.

1. Khalil, H. H., Mac Keith, R. C. *Brit. med. J.* 1954, ii, 734.
2. Barnard, C. N. *Brit. J. Surg.* 1956, **44**, 296.
3. Khalil, H. H. *Lancet*, 1956, i, 1092.
4. Khalil, H. H. *Proc. R. Soc. Med.* 1957, **56**, 78.
5. Kh il, H. H. *Lancet*, 1957, **1**, 185.

CHRISTMAS GIFTS FUND APPEAL

SIR,—Every autumn an appeal is made to members of the medical profession for contributions to the Christmas Gifts Fund organised by the Royal Medical Benevolent Fund.

To receive a gift at Christmas time is a joy to everyone, but particularly to those who are lonely or in need. To none is a gift more welcome than to those who have fallen on hard times.

Our beneficiaries include colleagues who have met with misfortune, and widows and children who are often in desperate need when their breadwinner has been taken before he was able to make provision for them. A gift at Christmas will enable them to enjoy some of the traditional good cheer of the season.

I ask your readers once again to give generously. Contributions marked Christmas Gifts should be sent to the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15.

HENRY TIDY
President, Royal Medical
Benevolent Fund.

Medicine and the Law

Death During Anæsthesia

AFTER having five teeth extracted a 6-year-old boy died from cardiac arrest due to shock resulting from a change in anæsthetics, it was stated at an inquest in Manchester on Oct. 2. The city coroner recorded a verdict of death by misadventure.

The dentist said he first administered nitrous oxide and then trichloroethylene. He made three extractions and noticed that the boy was regaining consciousness. For five seconds he administered ethyl chloride and took out two more teeth. The boy's respiration became shallow and he was given oxygen, but he collapsed and died.

Replying to the coroner, the dentist said he knew there was a strong opinion among dentists about the dangers of trichloroethylene and ethyl chloride, but he did not think there was any risk in that case as the boy was strong and healthy. He agreed, however, that there would have been less risk if he had continued to administer the nitrous oxide. In his opinion it was the ethyl chloride that caused the boy's death.

A consultant anæsthetist said that what the dentist had done was widely practised provided patients were not susceptible to a sudden change in anæsthetics. To some patients, such as invalids or young children, trichloroethylene could be dangerous and ethyl chloride slightly more dangerous. He considered it would have been safer to have kept on with the nitrous oxide.

Obituary

DAVID NUNES NABARRO

M.D., B.Sc. Lond., F.R.C.P., D.P.H.

Dr. David Nabarro, who died on Oct. 3 at the age of 84, was for over twenty years director of the pathology department of The Hospital for Sick Children, Great Ormond Street. His reputation as an expert in the treatment and diagnosis of congenital syphilis was firmly founded on the experience he had gained at the pioneer venereal-diseases clinic which he established at the hospital.

He was the son of Jacob Nabarro a London merchant, and he was educated at Owens' School, Manchester, and at University College, London, where he graduated B.SC. in 1893. He continued his medical studies at University College Hospital, qualifying in 1897. Two years later he proceeded to the degree of M.D. and was awarded the university gold medal. He was also appointed assistant professor of pathology and bacteriology, and he held this appointment till 1910.

His work in London was interrupted in 1903 when he visited Uganda as a member of the Royal Society's commission and, with the late Sir David Bruce and Prof. Aldo Castellani, was one of the co-discoverers of the cause and mode of transmission of sleeping-sickness. Of this early interest P. M.-B. writes:

"Nabarro often spoke earnestly and feelingly of his contributions to pioneer tropical medicine when working with the commission in Uganda. He did an immense amount of detailed work, under the direction of Sir David Bruce, for which he later received little recognition. This ended his career in tropical medicine, but, though wedded to bacteriology, he continued to make himself familiar with the major advances in this subject, and he was a familiar figure at scientific meetings. Though naturally shy and retiring he was very popular. This was due to his friendly personality and efficiency coupled with innate modesty. His small figure appeared to be dominated by a pair of dark, sparkling and inquiring eyes matching a quizzical and puckish expression."

In 1910 he became pathologist to the Evelina Hospital for Children, and in 1912 he joined the staff at Great Ormond Street; and the rest of his professional career was centred on the hospital. He was largely responsible for starting the biochemical laboratory, and in 1917 he initiated a venereal-diseases clinic. In 1920 he was appointed director of the hospital's pathological department; and his interpretation of his duties as director was to use his best endeavours, in committee and out, to see that adequate facilities for his actively growing department were forthcoming—a task which at the time was difficult owing to financial stringency. With the end of the depression the opportunity of building a new hospital came, and he was able to put his dreams on paper and to see them grow into reality; he moved into the fine new laboratories which he had planned, in the heart of the new hospital, before he retired in 1939. Soon afterwards the war broke out, and he joined the Emergency Pathological Service and continued to work till the end of the war. Afterwards he set himself the task of writing a monograph on *Congenital Syphilis* based on his long experience. This was published in 1954; and in the same year, to mark his 80th birthday, his colleagues at the hospital presented him with 18th-century tea caddies, teapot, teacup, and saucer, and a 20th-century tea alarum. The personality which inspired this unorthodox but affectionate gift is described by W. W. P.:

"Besides his obvious duties as director Nabarro had three main interests. The chief of these was his clinic which was the first children's clinic set up in England for the study and treatment of congenital venereal disease. His next interest was a continuation of a study which he had been carrying on for years, on the aberrant types of coli organisms, and he to a considerable extent duplicated the work which was published by Sonne. His third interest was philately, and, if one went to his office after hours of an evening, one would more often than not find him poring over a collection of stamps which he had received from one of his many correspondents in all corners of the British Empire. As a colleague he was charming and he was gifted with a good sense of humour. He had a wide fund of reading by no means limited to pathology, and he was always prepared to help one with references, or, equally important, knew where to find them when one had problems to solve. He was remarkably alert and quick in his movements, and this he retained to the last few years of his life; in fact one frequently had considerable difficulty in keeping up with him, particularly in the winding corridors of the old hospital when visiting patients together. It seems strange to think that we shall no longer see him popping around one or other corner of the hospital."

Dr. Nabarro married in 1914 Florence Nora, daughter of Nathan Bell Webster of North Walsham. She survives him with a daughter and a son, Dr. J. D. N. Nabarro.

MARIE CARMICHAEL STOPES

D.Sc. Lond., Ph.D. Munich, F.L.S., F.G.S., F.R.S.I.

Dr. Marie Stopes, president of the Society for Constructive Birth Control and Racial Progress, died at her home, Norbury Park, near Dorking, on Oct. 2 at the age of 78.

She was the daughter of Henry Stopes, an anthropologist, and she was a student at University College, London, where she gained the gold medal in botany and graduated B.SC. with first-class honours. Later she took her D.SC. degree, and after further study under Goebel and Radelkofer graduated PH.D. from the University of Munich. In 1904 she joined the faculty of science of the University of Manchester. Three years later she made a long visit to Japan, where she worked at the Imperial University, Tokyo, and explored the country collecting fossils and plants. On her return she was appointed lecturer in palæobotany at Manchester.

To the end of her life Dr. Stopes continued her scientific work and interests, but outside a small group of fellow specialists she was of course more widely known for her writings on birth-control. Her earliest book on this subject, *Married Love*, appeared in 1918, and it was then described in our columns as

"an extremely sensible little book; it deals in the most intimate way with normal sexual life and by sheer frankness remains decent. Of the things which are commonly accepted as sound physiology we need only say that they are also things which thousands of people would be happier for knowing . . . the book is really needed as a public adviser."

These words written thirty years ago sum up not too inadequately Dr. Stopes' contribution to sexual education. Her simplicity and directness made it available for the first time to the people who perhaps needed it most. Many working-class mothers were also grateful for her practical help; for in 1921, with Mr. Humphrey Verdon Roe, the aircraft pioneer whom she had married three years before, she set up the Mothers' Clinic in Holloway. Other early clinics were opened, not always without

opposition, in other large towns, and to begin with were often maintained by the generosity of Dr. Stopes and her husband.

Dr. J. W. BROWN

T. H. S. writes:

"Jimmy Brown was one of the most human of physicians and achieved a unique position, not dissimilar to that of James Mackenzie. He spent nearly fifteen years in general practice before becoming a consultant in cardiology. His classic publication on *Congenital Heart Disease* never received the recognition it should have had, probably because it was originally published before the advent of surgery of the heart and was consequently of less interest than it would be now. Later editions, however, show how sound were the observations and conclusions made at the bedside by a man who put the welfare of his patients before everything."

Diary of the Week

OCT. 12 TO 18

Monday, 13th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5.15 P.M. Mr. F. B. Cockett: Post-Thrombotic Syndrome of the Leg.
6.30 P.M. Mr. Clive Butler: Carcinoma of the Colon.

UNIVERSITY OF LONDON
5.30 P.M. (St. Bartholomew's Hospital Medical College, E.C.1.) Prof. W. F. Hamilton (Augusta, Georgia): Measurements of the Cardiac Output. (First of three lectures.)

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Prof. J. Chassar Moir: Thoughts on the Technique of Cæsarean Section.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
5 P.M. Dr. B. G. B. Lucas: Artificial Aids in the Control of the Circulation. (Bengué lecture.)

Tuesday, 14th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Mr. H. C. Edwards: Disorders of the Jejuno-ileum.
6.30 P.M. Mr. W. P. Cleland: Surgical Treatment of Acquired Valvular Disease of the Heart.

UNIVERSITY OF LONDON
5.30 P.M. (St. Bartholomew's Hospital Medical School.) Professor Hamilton: Regulation of the Cardiac Output. (Second of three lectures.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Dr. A. G. Bearn, Dr. J. N. Cumings, Dr. G. Curzon: Wilson's Disease.
8 P.M. *Psychiatry.* Dr. Eliot Slater: Problems of Pathography. (Presidential address.)

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Prof. Gordon Lennon: Modern Treatment of Heart-disease in Pregnancy.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
2 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Colonel P. H. Addison: Legal Hazards in Obstetrics and Gynæcology.
3 P.M. Prof. C. V. Harrison: Obstetric Anuria.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. R. H. Meara: Sweat Production and Anomalies.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) Prof. W. I. C. Morris: John and William Hunter and their Polemics.
8 P.M. *Surgery.* (Staff House, University of Manchester.) Mr. H. T. Cox: The Dumping Syndrome. (Presidential address.)

Wednesday, 15th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Mr. S. M. Cohen: Place of Sympathectomy Procedures.
6.30 P.M. Mr. John Charnley: Fractures of the Femur.

UNIVERSITY OF LONDON
5.30 P.M. (St. Bartholomew's Hospital.) Professor Hamilton: Experimental Congestive Failure of the Circulation. (Last of three lectures.)

ROYAL SOCIETY OF MEDICINE
8.15 P.M. *General Practice.* Dr. G. M. Kerr: Dos and Don'ts in Dental Dopes. (Valedictory address.)

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Histology of Normal Skin.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. A. B. Paterson: Development and Detection of Tuberculin Sensitivity.

BRITISH ASSOCIATION OF SPORT AND MEDICINE
5.30 P.M. (Charing Cross Hospital Medical School, Chandos Place, W.C.2.) Mr. Frank Law, Mr. M. J. Roper-Hall: Vision in Sport.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Dr. Christopher Tietze: Human Fertility—Statistical Considerations.

MIDLAND MEDICAL SOCIETY
8.45 P.M. (Birmingham Medical Institute, 36, Harborne Road, Edgbaston.) Dr. T. F. Fox: Rewards and Fairies.

UNIVERSITY OF LIVERPOOL
5.15 P.M. *Medical Faculty.* Prof. I. F. S. Mackay (Jamaica): Measurement of Arterial and Venous Valvular Incompetence.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH, Nicolson Street, Edinburgh, 8
3.30 P.M. Mr. C. P. Wilson: Diverticula of the Pharynx.

Thursday, 16th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Mr. H. R. I. Wolfe: Testicular Tumours.
6.30 P.M. Mr. Ashton Miller: Diverticula of the Bladder.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (Senate House, University of London, Malet Street, W.C.1.) Sir Edward Salisbury: Influence of Botany on Health and Disease. (First lecture of series on Scientific Basis of Medicine.)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Sir Philip Manson-Bahr: The March of Tropical Medicine During the Last Fifty Years. (First Manson oration.)

HYPNOTHERAPY GROUP
8 P.M. (1, Wimpole Street, W.1.) Dr. Lindesay Neustatter: Homosexuality.

NORTH WESTERN THORACIC SOCIETY
5 P.M. (Clinical Science Buildings, Manchester.) Dr. Robert Coope: Sundry and Manifold Changes. (Presidential address.)

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. D. V. Hubble: Auto-immunising Thyroiditis.

Friday, 17th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
3 P.M. Sir Geoffrey Keynes: Harvey Through John Aubrey's Eyes. (Harveian oration.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Mr. G. C. Knight: Cervical Disc Lesions.
6.30 P.M. Mr. Ralph Shackman: Non-tuberculous Urinary Infections.

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Epidemiology and Preventive Medicine.* Brigadier Sir John Boyd, Dr. E. M. Mackay-Scollay, Dr. E. T. Conybeare: Tetanus.
8.15 P.M. *Radiology.* Dr. John Fawcitt, Mr. H. A. Maslowski: Radiological and Neurosurgical Aspects of Congenital Anomalies of the Spine in Childhood and Infancy. Mr. Kenneth Till: Observations on Spinal Tumours in Childhood.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. N. Asherson: Deafness.

MANCHESTER MEDICAL SOCIETY
5 P.M. (Clinical Sciences Building, York Place.) *Section of Anæsthetics with North of England Society of Obstetricians and Gynæcologists.* Dr. A. Mackenzie, Dr. E. G. Rees Jones, Dr. H. E. Pooler, Dr. Trevor Johnson, Mr. O. Vaughan Jones, Prof. T. N. A. Jeffcoate: Anæsthesia in Obstetrics.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW
8.30 P.M. *With the Medico-Chirurgical Society of Edinburgh.* (Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow, C.2.) Prof. M. F. A. Woodruff, Mr. Robert Mailer, Dr. J. D. S. Cameron: The Relative Importance of the Scientific and The Clinical in Medical Training.

Appointments

BURGOYNE, JOHN, M.B. Glasg., F.F.A.R.C.S., D.A.: consultant anæsthetist, South-Eastern Regional Hospital Board central group of hospitals, Scotland.

CHALMERS, T. S., M.B. Edin., F.R.C.S.E.: consultant surgeon, West Fife board of management hospitals.

CLARKE, M. F. J., L.R.C.P.E.: assistant senior M.O., Oxford.

DAWSON, R. L. G., M.B. Lond., F.R.C.S.: plastic surgeon, Royal Free Hospital, London.

DUNN, A. S., L.R.C.P.E., D.C.H.: assistant divisional M.O., Lancashire.

FAIRWEATHER, SHEILA H. E., M.B. Lpool, D.P.H., D.C.H.: assistant M.O. Finchley and Hendon.

FLOOD, C. M., M.D. Lond., M.R.C.O.G.: part-time assistant to the director of the department of obstetrics, Guy's Hospital London.

FOSTER, C. A., M.B. Lond., F.F.A.R.C.S., D.A.: anæsthetist, St. Thomas's Hospital, London.

GATHERER, ALEXANDER, M.B. Aberd., D.P.H.: deputy M.O.H. and deputy principal school M.O., Warrington.

GRAHAM, M. V., M.B. Dubl., F.R.C.S., D.O.M.S.: consultant ophthalmologist, United Cardiff Hospitals and regional board hospitals.

MITCHELL, F. L., M.B. Lpool, D.C.H.: assistant maternity and child welfare M.O., Durham.

MORWOOD, J. B., M.B. Belf., F.R.C.S.I., D.P.H.: deputy divisional M.O., north central division, Surrey, and M.O.H., Malden, Coombe, and Esher.

MURRAY, B. T. A., M.B. N.U.I., D.P.H., D.C.H.: assistant divisional M.O., Lancashire.

PINKERTON, J. R. H., M.D. Cantab.: consultant pathologist-in-charge, Lincoln and Grantham group of hospitals.

PRACY, ROBERT, M.B. Lond., F.R.C.S.: consultant otorhinolaryngologist (junior status), Liverpool Ear, Nose, and Throat Infirmary.

PREISKEL, ELLA, M.B. Lond., D.M.R.: consultant radiologist, X-ray diagnostic department, Elizabeth Garrett Anderson Hospital, London.

WAGG, AUDREY, M.B. Durh.: assistant maternity and child welfare M.O., Durham.

*WHITFIELD, AUDREY P., M.B. Lond.: principal M.O., Middlesex.

* Amended notice.

Manchester Regional Hospital Board:

BUCKLEY, R. W., M.B. Manc., F.F.A. R.C.S.: consultant anæsthetist, Macclesfield and district group of hospitals.

CALVERT, R. J., M.D. Glasg., M.R.C.P.: consultant physician, Burnley and district group of hospitals.

CARR, J. A., M.D. Durh., F.R.C.S.: consultant surgeon, Bury and Rossendale group of hospitals.

DANZIGER, A. M., M.R.C.S., D.A.: assistant anæsthetist (S.H.M.O.), north Manchester group of hospitals.

DAVIES, C. St. J., M.R.C.S., D.M.R.D.: consultant radiologist, Stockport and Buxton group of hospitals.

DAWS, R. A., F.R.C.S.: consultant neurosurgeon based on Preston and Lancaster.

KEATING, W. J., M.B. N.U.I., F.F.A. R.C.S.: consultant anæsthetist, Burnley and district group of hospitals.

OAKLEY, D. P., M.B. Manc., D.P.M.: assistant psychiatrist (S.H.M.O.) Whittingham Hospital.

O'NEILL, JOHN, M.B. Durh., M.R.C.P., D.P.M.: consultant psychiatrist, Ashton, Hyde, and Glossop group of hospitals and Parkside Hospital.

TENNANT, HELEN L. S., M.B. Manc., D.A.: assistant anæsthetist (S.H.M.O.), north Manchester group of hospitals.

WADDINGTON, G. H., M.R.C.S., D.M.R.D.: consultant radiologist, Bolton and district group of hospitals.

Notes and News

DOCTORS' WINDOW IN GUILDFORD CATHEDRAL

THE Guildford division of the British Medical Association has undertaken to raise sufficient funds to provide, as a gift from the medical profession, one of the lancet windows of the new Guildford Cathedral, now nearly complete. Dr. G. I. Watson, chairman of the division, appeals to all doctors "who wish to hasten the completion of this great new church" to send a donation to the Doctors' Cathedral Window Fund, c/o the Treasurer, Dr. F. A. Belam, 1, Westfield, Epsom Road, Guildford, Surrey.

University of Birmingham

The following appointments have been announced:

Sir Francis Knowles, Dr. Alan Glass, and Dr. A. W. Rogers, lecturers in anatomy; Dr. H. A. Ellis, and Dr. D. J. Parish, lecturers in pathology; Dr. J. D. Cumming, lecturer in physiology; Dr. S. H. Taylor, lecturer in medicine; Mr. G. T. Watts, lecturer in surgery; Mr. Frank Ashton, lecturer in surgery; Dr. E. M. Little, lecturer in obstetrics and gynæcology; Dr. June Lloyd, research fellow in pædiatrics and child health.

Royal College of Surgeons of England

On Thursday, Oct. 30, at 5 P.M., at the college, Lincoln's Inn Fields, London, W.C.2, Sir John McNee will give the Thomas Vicary lecture. His subject will be Barber-Surgeons in Great Britain and Ireland.

King's College Hospital, London

On Oct. 1 new medical and surgical units at the medical school were inaugurated. Dr. Clifford Hoyle has been appointed part-time director of the medical unit, and Mr. Harold Edwards has been appointed part-time director of the surgical unit.

College of General Practitioners

South London Faculty.—On Friday, Oct. 31, at 8.45 P.M., at King's College Hospital Medical School, Denmark Hill, S.E.5, Prof. J. S. Mitchell will give a lecture on nuclear fission in relation to medicine.

Northern Home Counties Faculty.—This faculty will hold a symposium on research in general practice on Wednesday, Nov. 5, at 8.30 P.M. at the George Hotel, Enfield.

Middlesex Hospital Medical School

At the annual dinner of the Middlesex Hospital Medical School on Oct. 3, Mr. Philip Wiles, the chairman, spoke of the death of Sir Ernest Kennaway, who had contributed so much to fundamental research into the ætiology of cancer, and of Lord Webb-Johnson: "The hospital as we know it now was his creation". Among alumni who had been honoured in the past year were Mr. E. W. Riches: "Never was a knighthood better deserved". During these twelve months there had been no change in the consultant staff; but one new post in physical medicine had been created. The exchange of staff with the University of Toronto was operating to the benefit of both parties. Mr. Wiles referred finally to Sir Gordon Gordon-Taylor, who had apparently discovered the gift of eternal youth; on his 80th birthday he had been presented with his portrait.

Prof. B. W. Windeyer, the dean, talked of the new building for the medical school. The need was great: at present there was not even enough room for the work on aldosterone, which had been discovered at the Middlesex by Dr. and Mrs. Tait. Phase 1 of construction was now assured; but they must start on phase 2, which was inseparable from the first phase. The third phase would include a residential college for 150 students, to be known as the Astor College. Dr. J. G. Walker, exercising the traditional privilege of the senior Broderip scholar to complain, renewed the plea that students should take a greater part in extracurricular activities. Finally Mr. P. H. Newman proposed The Chairman, speaking of him with long knowledge and esteem. Mr. Wiles, he insisted, was "the arch-enemy of complacency".

North East London Clinical Society

Meetings of this society will be held at the Prince of Wales' Hospital, Tottenham, N.15, at 2.30 P.M. on Thursdays, Oct. 23, Nov. 20, Jan. 22, Feb. 19, and March 19.

Pharmaceutical Society of Great Britain

On Wednesday, Oct. 22, at 7.30 P.M., at 17, Bloomsbury Square, London, W.C.1, Dr. A. H. Beckett will give a lecture on pharmaceutical research in the United States.

Symposium on Cancer

A symposium on recent advances in cancer is to be held at the Royal Marsden Hospital, Fulham Road, London, S.W.3, on Saturday and Sunday, Oct. 25 and 26. The course, which is intended for junior consultants, S.H.M.O.s, and senior registrars, is the first of its kind to be held at the hospital.

Abortion Law Reform Association

This Association will hold a meeting at Caxton Hall, Westminster, S.W.1, at 7.15 P.M., on Wednesday, Oct. 22, when Prof. Glanville Williams, LL.D., Miss D. M. Kerslake, M.R.C.O.G. and Mrs. Lena Jeger, M.P., will speak on the new Medical Abortion Bill.

Queen's Institute of District Nursing

This Institute is holding a conference on Thursday, Oct. 23, at 2.30 P.M. at Caxton Hall, London, S.W.1, to discuss accidents in the home. The speakers will include Mr. John Watson, F.R.C.S.E. The annual meeting of the Institute will be held on Thursday, Nov. 27, at 2.30 P.M. at Church House, London, S.W.1. Tickets for both meetings can be had from the Institute, 57, Lower Belgrave Street, S.W.1.

New Record for Blood Donors

The number of blood donors enrolled in England and Wales at the end of June was 690,356, compared with 674,117 at the end of December, 1957. In 1946 the total was only 267,000. During the past ten years supplies of blood to hospitals have almost doubled—from 371,000 bottles in 1949 to 735,000 in 1957. During the first half of this year 383,750 bottles were issued.

Leicester Christian Medical Association

This society will hold its first meeting of the new session on Friday, Oct. 17, when Mr. S. G. Browne, F.R.C.S., will speak on sunshine and shadow in the African equatorial forest. Other speakers during the session will include Mr. Stuart Mawson, F.R.C.S., Mr. Cedric Harvey, F.R.C.S., Dr. Kobina Taylor, Rev. R. De C. Allen, and Rev. F. S. Sinker, M.R. All the meetings will be held in the Leicester Royal Infirmary at 8.45 P.M. Further particulars may be had from the secretary, Dr. J. P. Anderson, 365, Uppingham Road, Leicester.

Colonel R. A. Smart, leader and medical officer of the Royal Society Antarctic Expedition for the International Geophysical Year, has been awarded the polar medal.

Dr. Alexander Walk, Dr. John Douglas, and Mr. J. Basil Hume have been appointed members of the General Nursing Council till 1963.

A meeting of the Biochemical Society will be held on Saturday, Oct. 18, at 2 P.M., at the Royal College of Science, London, S.W.7.

The current (September) issue of *Health Education Journal* contains a report of the conference on children going into hospital which the Central Council for Health Education arranged in January. The report includes a synopsis of the paper which Prof. R. S. Illingworth read at the conference and which was later published in full in our columns (*Lancet*, July 26, p. 165).

The Central Mediterranean Forces Surgeons' Club will hold its annual dinner on Saturday, Nov. 1, at 7.45 P.M., at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2. Tickets (£2) may be had from the secretary of the club, Mr. Harold Burge, 73, Bathgate Road, S.W.19.

CORRIGENDUM: *Rehabilitation in Psychiatry.*—Dr. Walter E. Barton, whose recent lecture in London we reported last week (p. 737), is superintendent of the *Boston* State Hospital. In the third paragraph of the report we wrongly ascribed to Dr. Barton an assertion that "Patients living apart from their families returned to hospital far more frequently".